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LOGINID:ssspta1626amd

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 09  JAPIO to be reloaded August 25, 2002
 NEWS 20  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 21  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 22  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)
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Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

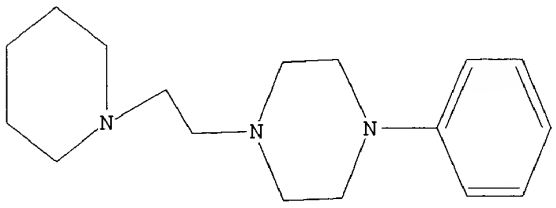
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09764710.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
FULL SEARCH INITIATED 13:22:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6501 TO ITERATE

100.0% PROCESSED 6501 ITERATIONS 317 ANSWERS
SEARCH TIME: 00.00.01

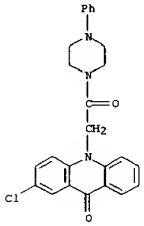
L2 317 SEA SSS FUL L1

=> s l2 and caplus/lc
23929408 CAPLUS/LC
L3 288 L2 AND CAPLUS/LC

=> s l2 not l3
L4 29 L2 NOT L3

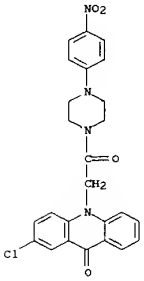
=> d 1-29

L4 ANSWER 1 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 420834-76-0 REGISTRY
CN Piperazine, 1-[(2-chloro-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 Cl N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



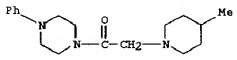
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 2 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 403716-00-7 REGISTRY
CN Piperazine, 1-[(2-chloro-9-oxo-10(9H)-acridinyl)acetyl]-4-(4-nitrophenyl)-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H21 Cl N4 O4
SR Chemical Library
LC STN Files: CHEMCATS



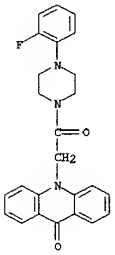
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 3 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 397880-89-6 REGISTRY
CN Piperazine, 1-[(4-methyl-1-piperidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX
NAME)
FS 3D CONCORD
MF C18 H27 N3 O
SR Chemical Library
LC STN Files: CHEMCATS



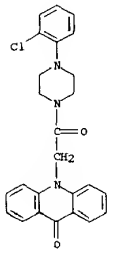
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 4 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-94-0 REGISTRY
CN Piperazine, 1-(2-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 F N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



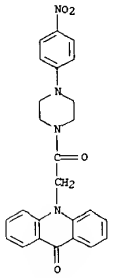
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 5 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-90-6 REGISTRY
CN Piperazine, 1-(2-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 Cl N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



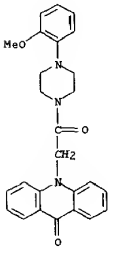
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 6 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-88-2 REGISTRY
CN Piperazine, 1-(4-nitrophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 N4 O4
SR Chemical Library
LC STN Files: CHEMCATS



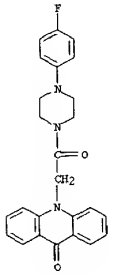
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 7 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-87-1 REGISTRY
CN Piperazine, 1-(2-methoxyphenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C26 H25 N3 O3
SR Chemical Library
LC STN Files: CHEMCATS



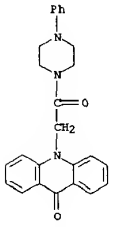
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 8 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-29-1 REGISTRY
CN Piperazine, 1-(4-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 F N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



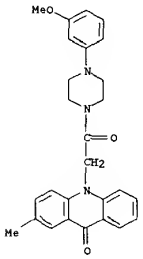
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 9 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 389577-27-9 REGISTRY
CN Piperazine, 1-[(9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H23 N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



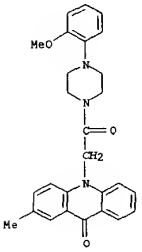
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 10 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362494-03-9 REGISTRY
CN Piperazine, 1-(3-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H27 N3 O3
SR Chemical Library
LC STN Files: CHEMCATS



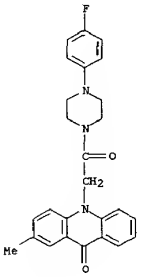
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 11 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362493-98-9 REGISTRY
CN Piperazine, 1-(2-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H27 N3 O3
SR Chemical Library
LC STN Files: CHEMCATS



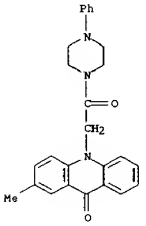
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 12 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362493-85-4 REGISTRY
CN Piperazine, 1-(4-fluorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H24 F N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



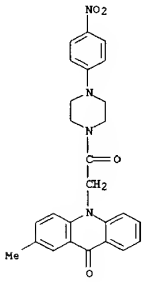
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 13 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362493-56-9 REGISTRY
CN Piperazine, 1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C26 H25 N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



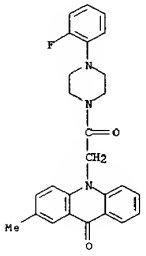
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 14 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362493-55-8 REGISTRY
CN Piperazine,
1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-(4-nitrophenyl)-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H24 N4 O4
SR Chemical Library
LC STN Files: CHEMCATS



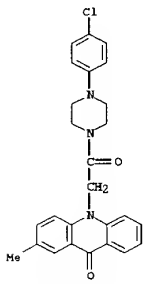
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 15 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 362493-49-0 REGISTRY
CN Piperazine,
1-(2-fluorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H24 F N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



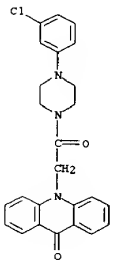
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 16 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 361197-24-2 REGISTRY
CN Piperazine,
1-(4-chlorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H24 Cl N3 O2
SR Chemical Library
LC STN Files: CHEMCATS



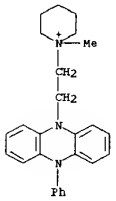
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 17 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 361188-24-1 REGISTRY
CN Piperazine, 1-(3-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-(9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 Cl N3 O2
SR Chemical Library
LC STN Files: CHEMCATS

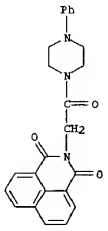


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 18 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 342603-26-3 REGISTRY
CN Piperidinium, 1-methyl-1-[2-(10-phenyl-5(10H)-phenazinyl)ethyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C26 H30 N3
CI COM
SR CA

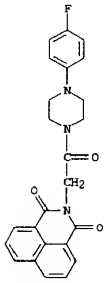


L4 ANSWER 19 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 326889-78-5 REGISTRY
CN Piperazine,
1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-phenyl-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H21 N3 O3
SR Chemical Library
LC STN Files: CHEMCATS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

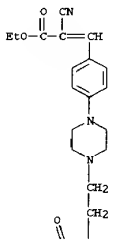
L4 ANSWER 20 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 326889-59-2 REGISTRY
CN Piperazine,
1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H20 F N3 O3
SR Chemical Library
LC STN Files: CHEMCATS



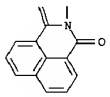
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 21 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 324774-78-9 REGISTRY
CN 2-Propenoic acid,
2-cyano-3-[4-[4-[2-(1,3-dioxo-1H-benz[de]isoquinolin-
2(3H)-yl)ethyl]-1-piperazinyl]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C30 H28 N4 O4
SR Chemical Library
LC STN Files: CHEMCATS

PAGE 1-A

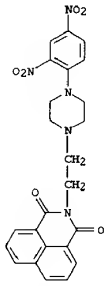


PAGE 2-A



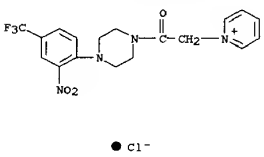
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 22 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 309735-93-1 REGISTRY
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2,4-dinitrophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H21 N5 O6
SR Chemical Library
LC STN Files: CHEMCATS



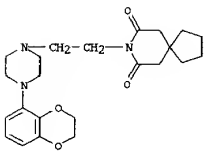
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 23 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 219139-24-9 REGISTRY
CN Pyridinium,
1-[2-[4-[2-nitro-4-(trifluoromethyl)phenyl]-1-piperazinyl]-2-oxoethyl]-, chloride (9CI) (CA INDEX NAME)
MF C18 H18 F3 N4 O3 . Cl
SR CAS Registry Services
LC STN Files: CHEMCATS



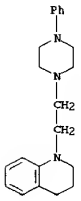
● Cl⁻

L4 ANSWER 24 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 171877-12-6 REGISTRY
CN 8-Azaspiro[4.5]decane-7,9-dione,
8-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H31 N3 O4
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

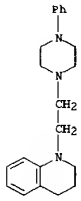
L4 ANSWER 25 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 112991-17-0 REGISTRY
CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride (6CI) (CA INDEX NAME)
MF C21 H27 N3 . Cl H
SR CAOLD
LC STN Files: CAOLD
CRN (110081-34-0)



● HCl

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 26 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 110081-34-0 REGISTRY
CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]- (6CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C21 H27 N3
CI COM
SR CAOLD
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)

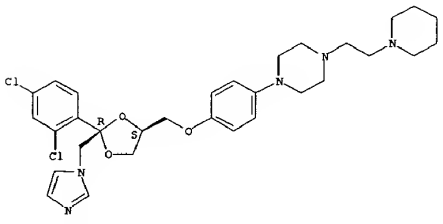


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

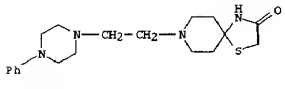
L4 ANSWER 27 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 75049-52-4 REGISTRY
CN Piperazine, 1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-4-[2-(1-piperidinyl)ethyl]-, cis- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H39 C12 N5 O3
CI COM

Relative stereochemistry.



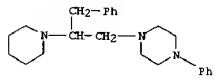
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 28 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 54950-44-6 REGISTRY
CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H28 N4 O S
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 29 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 7029-67-6 REGISTRY
CN Piperazine, 1-phenyl-4-(3-phenyl-2-piperidinopropyl)- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H33 N3
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       190.48     190.69

FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002
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FILE COVERS 1907 - 20 Aug 2002  VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002  (20020819/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d his

     (FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002
L1             STRUCTURE UPLOADED
L2          317 S L1 FUL
L3          288 S L2 AND CAPLUS/LC
L4           29 S L2 NOT L3

     FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002

=> s l3
L5          211 L3

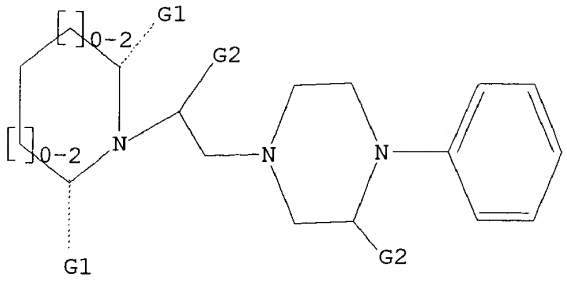
=>
Uploading 09764710.str

L6       STRUCTURE UPLOADED

=> s
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):end
```

SEARCH ENDED BY USER

=> d
L6 HAS NO ANSWERS
L6 STR



G1 H,O,S

G2 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	2.77	193.46

FILE 'REGISTRY' ENTERED AT 13:26:55 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s l6 subset=l2 ful
FULL SUBSET SEARCH INITIATED 13:27:08 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 317 TO ITERATE

100.0% PROCESSED 317 ITERATIONS 265 ANSWERS
SEARCH TIME: 00.00.01

L7 265 SEA SUB=L2 SSS FUL L6

=> s l7 not l2
L8 0 L7 NOT L2

=> s l7 and caplus/lc
23929408 CAPLUS/LC
L9 255 L7 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 37.43 230.89

FILE 'CAPLUS' ENTERED AT 13:27:34 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l9
L10 194 L9

=> fil reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.40 231.29

FILE 'REGISTRY' ENTERED AT 13:27:59 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s l7 ful
FULL SEARCH INITIATED 13:28:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6498 TO ITERATE

100.0% PROCESSED 6498 ITERATIONS 481 ANSWERS
SEARCH TIME: 00.00.01

L11 481 SEA SSS FUL L6

=> s l11 and caplus/lc
23929408 CAPLUS/LC
L12 444 L11 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	144.66	375.95

FILE 'CAPLUS' ENTERED AT 13:28:54 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l12
L13 263 L12

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.40	376.35

FILE 'CAPLUS' ENTERED AT 13:29:27 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l13
L14 263 L12

=> d 1-263 ibib abs hitstr

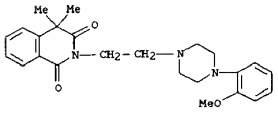
L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:521523 CAPLUS
DOCUMENT NUMBER: 137:73273
TITLE: Adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain
INVENTOR(S): Gil, Daniel W.; Aoki, Kei Roger
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053177	A2	20020711	WO 2001-US48651	20011214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-751053 A 20001229
OTHER SOURCE(S): MARPAT 137:73273
AB Agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically effective amt. of the agent, are disclosed. The agent may include a clostridial neurotoxin, a fragment or a deriv. thereof, attached to a targeting component, wherein the targeting component is selected form a group consisting of compds. which selectively binds at the .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptor subtype(s) as compared to other binding sites, e.g. the .alpha.2a adrenergic receptor subtype.
IT **67339-62-2D**, ARC 239, conjugates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



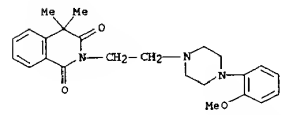
L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:408903 CAPLUS
DOCUMENT NUMBER: 136:395968
TITLE: Remedies for digestive functional disorder and screening method
INVENTOR(S): Yamamoto, Osamu
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042765	A1	20020530	WO 2001-JP10152	20011121

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-356040 A 20001122
AB Medicinal compns. contg. as the active ingredient an adrenergic .alpha.2B receptor selective antagonist, an adrenergic .alpha.2C receptor selective antagonist or an adrenergic .alpha.2B/2C receptor selective antagonist; and a method of screening the same. Namely, medicinal compns. for treating irritable bowel syndrome which have an excellent effect of improving enteric movement and a high safety; and a method useful in screening the same.
IT **67339-62-2**, ARC239
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adrenergic .alpha.2 B and C antagonists as remedies for digestive functional disorder and screening method)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:392232 CAPLUS
DOCUMENT NUMBER: 136:401912
TITLE: Nitrosated and nitrosylated alpha-adrenergic receptor antagonist compounds, compositions and their uses
INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saenz de Tejada, Inigo
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 714,313.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

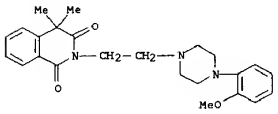
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061879	A1	20020523	US 2001-24550	20011221
US 5932538	A	19990803	US 1996-595732	19960202
US 5994294	A	19991130	US 1996-714313	19960918
PRIORITY APPLN. INFO.:			US 1996-595732 A2	19960202
			US 1996-714313 A2	19960918
OTHER SOURCE(S):		MARPAT 136:401912		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to nitrosated or nitrosylated a-adrenergic receptor antagonists, e.g. I [Ra = H, alkoxy; Rb = NMe(CH2)aNHCORc, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl; a= 2, 3; Rc = heteroaryl, heterocycle, lower alkyl, hydroxyalkyl, arylheterocycle; D = NO, NO2, C(Rd)OC(O)YZ(CReRf)pTQ; Rd = H, lower alkyl, cycloalkyl, aryl aralkyl, heteroaryl; Y = O, S, C, NRi; Ri = H, lower alkyl; Re, Rf = H, lower alkyl, haloalkyl, cycloalkyl, alkoxy, aryl, heteroaryl, NH2, (di)alkylamino, amido, CO2H, ester, TQ; ReRf = carbonyl, heterocycle, cycloalkyl; p = 1 - 10; T = bond, O, S, N; Z = bond, lower alkyl, haloalkyl, cycloalkyl, aryl, (CReRf)p, Q = NO, NO2], II [R = CH2N(C6H4Me-4)C6H4OD1-3, CH2Ph, 2-methoxy-1,4-benzodioxin-2-yl, 1-methyl-2,3-dihydroisoindol-2-yl, 5-chloro-2,3-dihydroisoindol-2-yl; D1 = H, D], III [Rh = H, C(O)ORd, C(O)X; X = Y(CReRf)pG(CReRf)pTQ; G = bond, TC(O), C(O)T, C(YC(O)Rm); Rm = heteroaryl, heterocycle], IV [A1 = O, CH2], V, (RmRkC)N(D1)(CRkR1) [Rk = H, lower alkly; R1 = CH2C6H4O(CH2)bMe, CH2C6H4OD, CH2OC6H3(OMe)2-2,6, CH2CH2Ph; b = 0, 1; Rn = CH2C6H4(SO2NH2)-3,

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
1-oxotetralin-2-yl, 1,4-benzodioxin-2-yl] and RpRkCHCH(Ro)OD [Ro = (1-naphthyloxy)methyl, C6H4OD1; Rp = 4-benzylpiperidino, 4-(2-methoxyphenyl)piperazino]. The present invention is also directed to compns. comprising .alpha.-adrenergic receptor antagonists that are optionally substituted with at least one NO or NO2 moiety and compds. that donate, transfer or release nitric oxide or elevate levels of endogenous endothelium-derived relaxing factor, and methods for treating sexual dysfunctions in males and females. Thus, S-Nitrosoglutathione was prepd. from glutathione via reaction with NaNO2 in aq. HCl. S-Nitrosoglutathione at 500 .mu.g was able to induce near maximal erectile response in anesthetized rabbits.
IT **67339-62-2D**, ARC 239, nitrosated or nitrosylated
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of nitrosated and nitrosylated alpha-adrenergic receptor antagonist compds., compns. and their uses)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



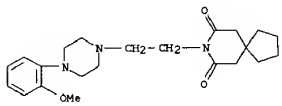
L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:368310 CAPLUS
DOCUMENT NUMBER: 136:363866
TITLE: Serotonergic compositions and methods for treatment of mild cognitive impairment
INVENTOR(S): Wurtman, Richard J.; Lee, Robert K. K.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038142	A2	20020516	WO 2001-US43016	20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-246615P P 20001108
AB A method of treating mild cognitive impairment is disclosed. The method comprises administering an effective amt. of a serotonergic agent, including, but not limited to, dexnorfenfluramine. The agent can be any serotonergic agonist, partial agonist, serotonin reuptake inhibitor, or combinations of these agents. The treatment method also encompasses combinations of serotonergic agents and nonsteroidal antiinflammatory agents. The treatment method may also delay the onset of mild cognitive impairment, dementia, or both.
IT **21102-95-4**, BMY 7378
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serotonergic compns. and methods for treatment of mild cognitive impairment)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

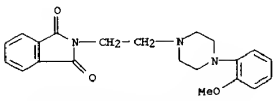
L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



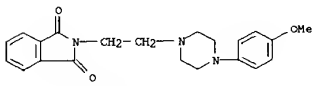
●2 HCl

L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:314042 CAPLUS
DOCUMENT NUMBER: 137:78925
TITLE: Design, synthesis and biological activity study on N-[4-(substituted phenyl)piperazine-1-yl]alkyl amide series as .alpha.1-adrenoceptor antagonists
AUTHOR(S): Fang, Hao; Xia, Lin; Jiang, Zhen-Zhou; Zhang, Wei; Zhang, Lu-Yong
CORPORATE SOURCE: Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Huaxue Xuebao (2002), 60(4), 725-731
CODEN: HHHPA4; ISSN: 0567-7351
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 137:78925
AB Novel furan-2-carboxylic acid {.omega.-[4-(substituted phenyl)-piperazine-1-yl]alkyl}amide and 2-oxo-2H-chromene-3-carboxylic acid {.omega.-[4-(substituted phenyl)piperazine-1-yl]alkyl}amide derivs. have been designed and synthesized based on the structure and activity relationship (SAR) of phenylpiperazine series as .alpha.1-adrenoceptor (.alpha.1-AR) antagonists and the results of computer-aided drug design we studied before. All the target compds. have been identified by 1H NMR, IR and MS (HRMS). Preliminary bioassay suggests that most of the target compds. display good blocking activity to .alpha.1-AR. The potency (pA2) of compd. N-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}-2-furancarboxamide is higher than prazosin.
IT **99718-67-9P 117046-73-8P 440117-82-8P**
440117-88-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. activity of phenylpiperazinylalkyl amides as .alpha.1-adrenoceptor antagonists)
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

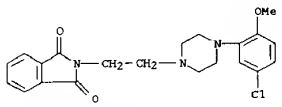
L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



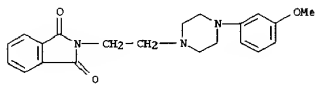
RN 117046-73-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 440117-82-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



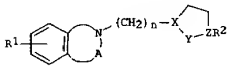
RN 440117-88-4 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:31419 CAPLUS
DOCUMENT NUMBER: 136:85830
TITLE: Preparation of bicyclic lactams and sulfonamides as 5-HT1A agonists
INVENTOR(S): Steiner, Gerd; Schellhaas, Kurt; Szabo, Laszlo; Behl, Berthold; Garcia-Ladona, Francisco Javier; Unger, Liliane
PATENT ASSIGNEE(S): Knoll Gmbh, Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002529	A1	20020110	WO 2001-EP7571	20010702
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10031391	A1	20020207	DE 2000-10031391	20000703

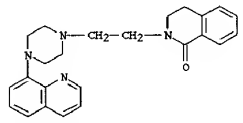
PRIORITY APPLN. INFO.: DE 2000-10031391 A 20000703
OTHER SOURCE(S): MARPAT 136:85830
GI



I

AB Title compds. [I; the ring including NA can be a 5-7 membered ring contg. O, S, or double bond; A = CO, SO2; X = N; Y = CH2, CH2CH2, (CH2)3, CH2CH; Z = N, C, CH; n = 2-4; R1 = H, halo, alkyl, CF3, OH, alkoxy, amino; R2 =

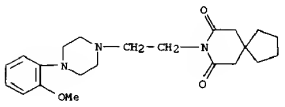
L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(substituted) (anellated) Ph, pyridyl, pyrazinyl] and salts thereof, were prepd. Thus, isoquinoline in DMF was stirred with NaH for 30 min. followed by addn. of 1-[4-(2-chloroethyl)-1-piperazinyl]isoquinoline (prepn. given) and stirring for 2 h at 80.degree. to give 82% 2-[2-(4-(1-isoquinolinyl)-1-piperazinyl)ethyl]-1(2H)-isoquinoline.2HCl.2H2O. Tested I showed affinity for the 5-HT1A receptor with Ki = 0.1-5.4 nM in HEK 293 cells.
IT **387399-38-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bicyclic lactams and sulfonamides as 5-HT1A agonists)
RN 387399-38-4 CAPLUS
CN 1(2H)-Isoquinolinone, 3,4-dihydro-2-[2-[4-(8-quinolinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:2436 CAPLUS
DOCUMENT NUMBER: 136:226674
TITLE: A-315456: a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity
AUTHOR(S): Buckner, Steven A.; Milicic, Ivan; Daza, Anthony; Lynch, James J.; Kolasa, Teodozyj; Nakane, Masaki; Sullivan, James P.; Brioni, Jorge D.
CORPORATE SOURCE: Abbott Laboratories, Abbott Park, IL, 60064-6118, USA
SOURCE: European Journal of Pharmacology (2001), 433(1), 123-127
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In functional assays, A-315456, N-[3-(cyclohexylidene-(1H-imidazol-4-ylmethyl))phenyl]ethanesulfonamide, behaved as an .alpha.1D-adrenoceptor subtype selective antagonist (pA2=8.34) in the rat aorta. It was 83-fold less potent at the .alpha.1B-adrenoceptor subtype expressed in the rat spleen, and was inactive at the .alpha.1A-adrenoceptor subtype expressed in the rat vas deferens. Radioligand binding assays also revealed high affinity (pKi=8.71) for the .alpha.1D-adrenoceptor subtype and weaker affinities at the .alpha.1A-adrenoceptor (pKi=6.23) and .alpha.1B-adrenoceptor (pKi=7.86). In comparison to its potent affinity at the .alpha.1D-adrenoceptor subtype, A-315456 was 3020-, 794- and 38-fold weaker at the dopamine D2-, 5-HT1A-, and .alpha.2a-adrenoceptors, resp. These studies indicate that A-315456 is a potent and selective .alpha.1D-antagonist that may serve as a useful pharmacol. ligand to probe the physiol. role of the .alpha.1D-adrenoceptor subtype in normal and disease states.
IT **21102-95-4**, BMY-7378 **255893-38-0**, SNAP 8719
RL: PAC (Pharmacological activity); BIOL (Biological study)
(A-315456, a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

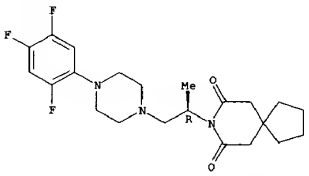
L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

RN 255893-38-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

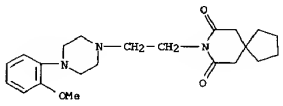
Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:789964 CAPLUS
DOCUMENT NUMBER: 136:64512
TITLE: Functional characterization of .alpha.1-adrenoceptor subtypes in human subcutaneous resistance arteries
AUTHOR(S): Jarajapu, Yagna P. R.; Johnston, Fiona; Berry, Colin; Renwick, Andrew; McGrath, John C.; MacDonald, Allan; Hillier, Chris
CORPORATE SOURCE: Vascular Assessment Unit, School of Biological and Biomedical Sciences, Glasgow Caledonian University, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(2), 729-734
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The functional characteristics of the .alpha.1-adrenoceptor subtypes in human resistance arteries are still not clear. The authors recently reported that the .alpha.1A-adrenoceptor predominantly mediates contraction to norepinephrine in human skeletal muscle resistance arteries. In this study the authors extended these investigations to human s.c. resistance arteries. Arterial segments were isolated from the inguinal s.c. fat and mounted on a small vessel wire myograph. Potencies of agonists and antagonists were examd. N-[5-(4,5-dihydro-1H-imidazol-2yl)-2-hydroxy-5,6,7,8-tetrahydronaphthalen-1-yl]methanesulfonamide (A-61603) was found to be 10- and 54-fold more potent than norepinephrine and phenylephrine, resp. Brimonidine (UK 14304) evoked significantly smaller contractile responses than norepinephrine and phenylephrine, showing the presence of a small population of .alpha.2-adrenoceptors in these arteries, and this was confirmed by the studies with selective .alpha.1- and .alpha.2-adrenoceptor antagonists prazosin and (8aR, 12aS, 13aS)-5,8,8a,9,10,11,12,12a,13a-decahydro-3-methoxyl-12-(ethylsulfonyl)-6H-isoquino[2,1-g][1,6]-naphthyridine (RS 79948). Prazosin, 5-methyl-urapidil, and 2-[2,6-dimethoxyphenoxyethyl]aminomethyl-1,4-benzodioxane (WB 4101) shifted the potency of norepinephrine concn. dependently giving pA2 values of 9.4, 8.9, and 10.1, resp., showing the presence of the .alpha.1A-subtype in these arteries. Pretreatment with 1

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and 10 .mu.M chloroethylclonidine did not affect the potency of and max. responses to norepinephrine, ruling out the presence of the .alpha.1B-subtype in these arteries. 8-[2-[4-(2-Methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7,9-dione (BMY 7378, 10 and 100 nM) did not affect the potency of norepinephrine but a small shift was obsd. by 1 .mu.M BMY 7378, giving a pKB value of 7.1, much less than that reported for the .alpha.1D-subtype. These results suggest the predominant involvement of .alpha.1A-adrenoceptor in the contractile responses to norepinephrine in these arteries. The physiol. role of this subtype in the maintenance of peripheral arterial resistance is yet to be confirmed.
IT **21102-95-4**, BMY 7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pharmacol. characterization of .alpha.1-adrenoceptor subtypes in human s.c. resistance arteries)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:781185 CAPLUS
DOCUMENT NUMBER: 135:328176
TITLE: Polymorphisms in human .alpha.2 adrenergic receptor
genes and their diagnostic and therapeutic uses
INVENTOR(S): Liggett, Stephen B.; Small, Kirsten M.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

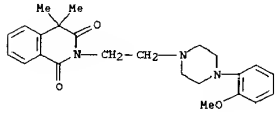
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079561	A2	20011025	WO 2001-US12575	20010417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-551744 A 20000417
US 2000-636259 A 20000810
US 2000-692077 A 20001019

AB The present invention includes polymorphisms in nucleic acids encoding the .alpha.2B, .alpha.2A, and .alpha.2C adrenergic receptor genes and expressed .alpha.2B, .alpha.2A and .alpha.2C adrenergic receptor protein mol. The invention also pertains to methods and mols. for detecting such polymorphisms. The invention further pertains to the use of such mols. and methods in the diagnosis and treatment of diseases such as cardiovascular and central nervous system disease. Genetic polymorphisms of deletion/insertions and single nucleotides in the intracellular loop 3 region of human .alpha.2 adrenergic receptors were identified and characterized to search for correlations between the polymorphisms and physiol. signaling functions of the receptors. Recombinant polymorphic receptor proteins were expressed in cell lines to measure ligand binding,

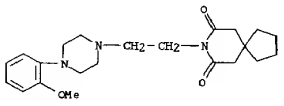
L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
protein phosphorylation, effect on adenyl cyclase activity, MAP kinase activation, GTP.gamma.S binding, and/or inositol phosphate accumulation.
Differences in signal transduction due to the .alpha.2 adrenoceptor polymorphisms were obsd. but the polymorphisms have not yet been genetically linked with disease, for example hypertension. The polymorphisms of this invention can be used to det. an individual's risk for developing a disease, for diagnosis, and for selecting appropriate drug treatments based on the identity of the polymorphism.
IT **67339-62-2**, ARC 239
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:776249 CAPLUS
DOCUMENT NUMBER: 137:433
TITLE: The hypotensive effect of BMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: Comparison with 8-hydroxy-dipropylamino tetralin
AUTHOR(S): Villalobos-Molina, Rafael; Lopez-Guerrero, J. Javier; Ibarra, Maximiliano
CORPORATE SOURCE: Departamento de Farmacobiologia, Centro de Investigacion y de Estudios Avanzados (CINVESTAV), Instituto Politecnico Nacional (IPN), Mexico City, 14000, Mex.
SOURCE: Archives of Medical Research (2001), 32(5), 389-393
CODEN: AEDEER; ISSN: 0188-4409
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stimulation of central 5-HT1A receptors produces bradycardia and diminishes blood pressure in conscious or anesthetized rats. Our objective was to investigate the effects on blood pressure and heart rate of the partial 5-HT1A receptor agonist and selective .alpha.1D-adrenoceptor antagonist BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl] ethyl]-8-azaspiro [4.5] decane-7,9 dione hydrochloride) compared to the full 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-dipropylamino tetralin) in adult anesthetized rats. Male Wistar rats of 6 mo of age were exposed i.v. (i.v.) to increasing doses of BMY 7378 or 8-OH-DPAT in the absence and presence of WAY 100635. Blood pressure and heart rate were continuously recorded. BMY 7378 induced a decrease in blood pressure with no apparent change in heart rate compared to basal values, while 8-OH-DPAT decreased both hemodynamic parameters. BMY 7378 hypotensive effect was antagonized by the selective, silent 5-HT1A receptor antagonist WAY 100635 (N-[2-[4-(2-methoxyphenyl)-1-piperazinyl] ethyl]-N-(2-pyridinyl) cyclohexanecarboxamide trihydrochloride). However, a remnant yet significant hypotensive effect was not blocked by the antagonist. In contrast, 8-OH-DPAT actions were completely blocked by WAY 100635. Data suggest that BMY 7378 cardiovascular effects are related to activation, as a full agonist, of central 5-HT1A receptors in adult rats; however, participation of other systems such as vascular .alpha.1-adrenoceptors in

L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
cardiovascular function is suggested.
IT **21102-95-4**, BMY 7378
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(hypotensive effect of BMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: comparison with 8-OH-DPAT)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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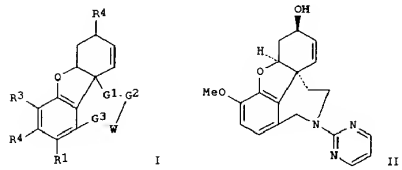
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:747793 CAPLUS
DOCUMENT NUMBER: 135:304054
TITLE: Preparation of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors
INVENTOR(S): Jordis, Ulrich; Froehlich, Johannes; Treu, Matthias; Hirnschall, Manfred; Czollner, Laszlo; Kaelz, Beate; Welzig, Stefan
PATENT ASSIGNEE(S): Sanochemia Pharmazeutika Aktiengesellschaft, Austria
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074820	A1	20011011	WO 2001-AT82	20010322
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1181294	A1	20020227	EP 2001-914813	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2001005563	A	20020402	BR 2001-5563	20010322
NO 2001005857	A	20020129	NO 2001-5857	20011130
PRIORITY APPLN. INFO.:			AT 2000-546	A 20000331
			AT 2001-238	A 20010215
			WO 2001-AT82	W 20010322

OTHER SOURCE(S): MARPAT 135:304054
GI

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



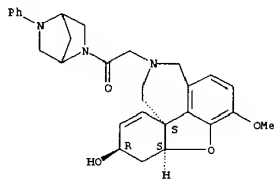
I II

AB Galanthamine derivs. and analogs, such as I [R1, R2 = H, Cn, OH, SH, NO2, SO3H, PO3H, NH2, halogen, etc.; R3 = OH, OMe; R4 = OH, alkyloxy, alkenyloxy, alkynyloxy, cycloalkyloxy, aryloxy, etc.; G1, G2, G3 = CH2, (CH2)2, (CH2)3, CH(OH), etc.; W = CH2, NR5, etc.; R5 = alkyl, acyl, aryl, etc.], were prepd. for therapeutic use as acetyl- and butyrylcholinesterase inhibitors. Thus, (.+-.)-galanthamine deriv. II was prepd. in 80.8% yield by condensation of (.+-.)-norgalanthamine with 2-chloropyrimidine using NaHCO3 in EtOH. The prepd. galanthamine derivs. and analogs were tested for acetyl- and butyrylcholinesterase inhibiting activity.

IT **365570-76-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors)
RN 365570-76-9 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane, 2-phenyl-5-[[(4aS,6R,8aS)-4a,5,9,10-tetrahydro-6-hydroxy-3-methoxy-6H-benzofuro[3a,3,2-ef][2]benzazepin-11(12H)-yl]acetyl]- (9Cl) (CA INDEX NAME)

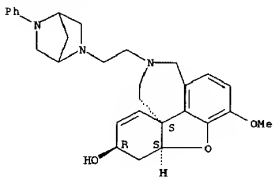
Absolute stereochemistry.

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT **365570-78-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors)
RN 365570-78-1 CAPLUS
CN 6H-Benzofuro[3a,3,2-ef][2]benzazepin-6-ol, 4a,5,9,10,11,12-hexahydro-3-methoxy-11-[2-(5-phenyl-2,5-diazabicyclo[2.2.1]hept-2-yl)ethyl]-, (4aS,6R,8aS)- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

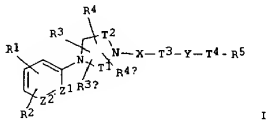


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

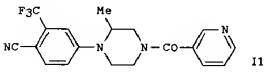
L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:704727 CAPLUS
DOCUMENT NUMBER: 135:257268
TITLE: Preparation of piperazinylbenzonitrile derivatives and analogs as antiandrogen agents
INVENTOR(S): Taniguchi, Nobuaki; Imamura, Masakazu; Kinoyama, Isao; Samizu, Kiyohiro; Kawanami, Eiji; Okada, Minoru; Kotoku, Hiroshi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001261657	A2	20010926	JP 2000-74999	20000317

OTHER SOURCE(S): MARPAT 135:257268
GI



I



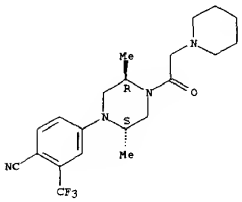
II

AB The title compds. I [R1, R2 = H, halo, etc.; R3, R3a, R4 , R4a = H, alkyl, etc.; T1 = (CH2)m; T2 = (CH2)n; T3 = (Alk1)p; T4 = (Alk2)q; R5 = (un)substituted carbamoyl, etc.; Alk1, Alk2 = (un)substituted alkylene, etc.; m, n = 1 - 3; p, q = 0 or 1; Z1, Z2 = CH, N; Y = bond, O, etc.; X = CO, etc.], useful as antiandrogen agents (no data), are prepd. For example, the title compd. II was prepd.

IT **362471-49-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

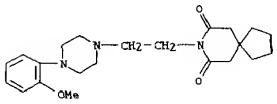
L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazinylbenzonitrile derivs. and analogs as antiandrogen
agents)
RN 362471-49-6 CAPLUS
CN Piperazine, 1-[4-cyano-3-(trifluoromethyl)phenyl]-2,5-dimethyl-4-(1-piperidinylacetyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:626800 CAPLUS
DOCUMENT NUMBER: 135:366874
TITLE: Molecular cloning and functional expression of the guinea pig .alpha.1a-adrenoceptor
AUTHOR(S): Gonzalez-Espinosa, C.; Romero-Avila, M. T.; Mora-Rodriguez, D. M.; Gonzalez-Espinosa, D.; Garcia-Sainz, J. A.
CORPORATE SOURCE: Departamento de Biologia Celular, Universidad Nacional Autonoma de Mexico, Instituto de Fisiologia Celular, Mexico City, 04510, Mex.
SOURCE: European Journal of Pharmacology (2001), 426(3), 147-155
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present paper, the cloning and expression of the guinea pig .alpha.1A-adrenoceptor is presented. The nucleotide sequence had an open reading frame of 1401 bp that encoded a 466 amino-acid protein with an estd. mol. mass of .apprxeq.51.5 kDa. When the clone was expressed in Cos-1 cells, specific high-affinity binding of [3H]prazosin and [3H]tamsulosin was obsd. Chloroethylclonidine treatment of membranes slightly decreased the total binding with both radioligands. Binding competition expts. using [3H]tamsulosin showed the following potency order: (a) for agonists: oxymetazoline.mchgt.epinephrine>norepinephrine>me thoxamine, and (b) for antagonists: prazosin.gtoreq.5-methyl-urapidil=benoxathian>phentolamine.mchgt.BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7,9-dione). Photoaffinity labeling using [125I-aryl]azido-prazosin revealed a major broad band with a mol. mass between 70 and 80 kDa. The receptor was functional, as evidenced by an epinephrine-increased prodn. of [3H]inositol phosphates that was blocked by prazosin.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(mol. cloning, functional expression and pharmacol. characterization of guinea pig .alpha.1a-adrenoceptor)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

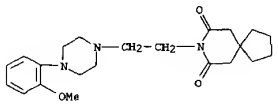


●2 HCl

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:522422 CAPLUS
DOCUMENT NUMBER: 135:327647
TITLE: Phe-308 and Phe-312 in transmembrane domain 7 are major sites of .alpha.1-adrenergic receptor antagonist binding: imidazoline agonists bind like antagonists
AUTHOR(S): Waugh, David J. J.; Gaivin, Robert J.; Zuscik, Michael J.; Gonzalez-Cabrera, Pedro; Ross, Sean A.; Yun, June; Perez, Dianne M.
CORPORATE SOURCE: Department of Molecular Cardiology NB5, The Lerner Research Institute, The Cleveland Clinic Foundation, Cleveland, OH, 44195, USA
SOURCE: Journal of Biological Chemistry (2001), 276(27), 25366-25371
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although agonist binding in adrenergic receptors is fairly well understood and involves residues located in transmembrane domains 3 through 6, there are few residues reported that are involved in antagonist binding. In fact, a major docking site for antagonists has never been reported in any G-protein coupled receptor. It has been speculated that antagonist binding is quite diverse depending upon the chem. structure of the antagonist, which can be quite different from agonists. We now report the identification of two phenylalanine residues in transmembrane domain 7 of the .alpha.1a-adrenergic receptor (Phe-312 and Phe-308) that are a major site of antagonist affinity. Mutation of either Phe-308 or Phe-312 resulted in significant losses of affinity (4-1200-fold) for the antagonists prazosin, WB4101, BMY7378, (+) niguldipine, and 5-methylurapidil, with no changes in affinity for phenethylamine-type agonists such as epinephrine, methoxamine, or phenylephrine. Interestingly, both residues are involved in the binding of all imidazoline-type agonists such as oxymetazoline, cirazoline, and clonidine, confirming previous evidence that this class of ligand binds differently than phenethylamine-type agonists and may be more antagonist-like, which may explain their partial agonist properties. In modeling these interactions with previous mutagenesis studies and using the current backbone structure of rhodopsin, we conclude that antagonist binding is docked higher in the pocket closer to the extracellular surface

L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
than agonist binding and appears skewed toward transmembrane domain 7.
IT **21102-95-4**, EMY7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(Phe-308 and Phe-312 in transmembrane domain 7 are major sites of .alpha.1-adrenergic receptor antagonist binding: imidazoline agonists bind like antagonists)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



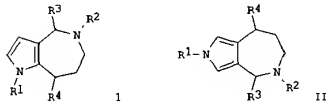
●2 MCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:502429 CAPLUS
DOCUMENT NUMBER: 135:92553
TITLE: Synthesis and activity of pyrroloazepine derivatives as 5-HT antagonists
INVENTOR(S): Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata, Norio
PATENT ASSIGNEE(S): Suntory Ltd., Japan
SOURCE: U.S., 54 pp., Cont.-in-part of U.S. Ser. No. 875,495.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6258805	B1	20010710	US 1999-312713	19990517
WO 9720845	A1	19970612	WO 1996-JP3522	19961202
W: AU, CA, HU, IL, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5962448	A	19991005	US 1997-875495	19970821
US 2002072515	A1	20020613	US 2001-801816	20010309

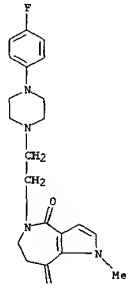
PRIORITY APPLN. INFO.: JP 1995-335714 A 19951201
JP 1996-46928 A 19960209
WO 1996-JP3522 W 19961202
US 1997-875495 A2 19970821
US 1999-312713 A1 19990517
OTHER SOURCE(S): MARPAT 135:92553
GI



AB Synthesis of pyrroloazepine derivs. (I) and (II) [R1 = H, alkyl, Ph, benzyl; R2 = substituted alkyl; R3,R4 independently = =O, =NOH, OH, OMe, SCH2CH2S] or pharmaceutically acceptable salts for use as 5-HT antagonists is disclosed. Thus, I [R1 = Me, R2 = (CH2)2-piperazinyl-C6H4F, R3 = =O, R4 = OH) (III) was prepd. by condensation of 3-pyrrolecarboxylic acid with .beta.-alanine Et ester hydrochloride, the amide ester sapond. and the

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
acid cyclized to pyrroloazepine with polyphosphoric acid, the azepine N alkylated with bromoalkylchloride followed by 1-(4-fluorophenyl)piperazine and redn. of carbonyl with NaBH4. III shows a 90.2% contraction at 10-7M in 5-HT action assay. I and II have strong serotonin-2 receptor antagonistic action and low toxicity and less side effects, and are therapeutically useful in the treatment of circulatory diseases and/or conditions related thereto.
IT **191591-85-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and activity of pyrroloazepine derivs. as 5-HT antagonists)
RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

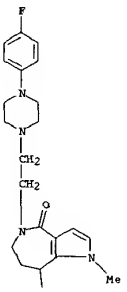


L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A

IT **191592-08-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of pyrroloazepine derivs. as 5-HT antagonists)
RN 191592-08-2 CAPLUS
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A



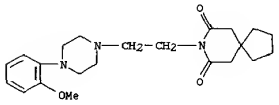
PAGE 2-A

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:473200 CAPLUS
DOCUMENT NUMBER: 135:283079
TITLE: Affinity of serotonin receptor antagonists and agonists to recombinant and native .alpha.1-adrenoceptor subtypes
AUTHOR(S): Yoshio, Rika; Taniguchi, Takanobu; Itoh, Harumi; Muramatsu, Ikunobu
CORPORATE SOURCE: Departments of Pharmacology and Radiology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: Japanese Journal of Pharmacology (2001), 86(2), 189-195
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding affinities of serotonin (5-HT)-receptor antagonists and agonists at human recombinant .alpha.1-adrenoceptor subtypes (.alpha.1a-, .alpha.1b- and .alpha.1d-subtypes) were examd. and compared with the functional affinities obtained in rat caudal artery (.alpha.1A-subtype), dog carotid artery (.alpha.1B-subtype) and rat thoracic aorta (.alpha.1D-subtype). Most of the 5-HT-receptor antagonists and agonists tested showed relatively high affinity to the three .alpha.1-adrenoceptor subtypes. The highest affinity (close to 1 nM) was found for NAN-190 (5-HT1A antagonist) in both binding and functional studies. 5-Methylurapidil (5-HT1A agonist) and BMY7378 (5-HT1A agonist) showed, resp., .alpha.1a(.alpha.1A)- and .alpha.1d(.alpha.1D)-subtype selectivity in both binding and functional affinities, but spiperone (5-HT2A antagonist) showed .alpha.1b-selectivity only in binding affinity. The functional affinity of ritanserin (5-HT2A antagonist) to the .alpha.1B-subtype was approx. 500-fold lower than that to the .alpha.1b-subtype. The results show that many 5-HT-receptor antagonists and agonists have high affinity for .alpha.1-adrenoceptors but suggest that there is a difference between their functional affinities and binding affinities in some cases.
IT **21102-95-4**, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(serotonin receptor antagonists and agonists affinity for .alpha.1-adrenoceptor subtypes in artery)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 17 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:434868 CAPLUS
DOCUMENT NUMBER: 135:29141
TITLE: Use of .alpha.1 adrenergic receptor subtype-selective drugs in patients with acute myocardial infarction
INVENTOR(S): Schwinn, Debra A.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

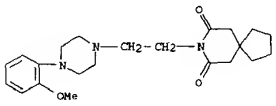
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041767	A1	20010614	WO 2000-US33135	20001207

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

US 2001031460	A1	20011018	US 2000-731062	20001207

PRIORITY APPLN. INFO.: US 1999-169294P P 19991207
AB The invention discloses the use of .alpha.1a adrenergic receptor-selective and/or .alpha.1a/.alpha.1d-selective antagonists in a method of preventing restenosis after myocardial infarction and reperfusion. The invention further discloses a method of identifying agents suitable for use in such a method.
IT **21102-95-4**, BMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.1 adrenergic receptor subtype-selective drugs in patients with acute myocardial infarction, and vascular distribution of .alpha.1 adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

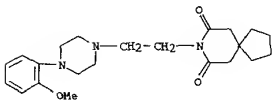
L14 ANSWER 17 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

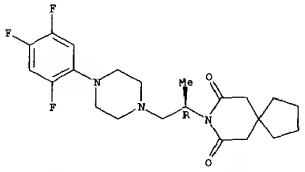
L14 ANSWER 18 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

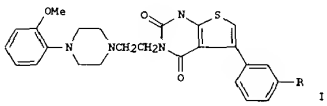
RN 255893-38-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 18 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:321149 CAPLUS
DOCUMENT NUMBER: 135:137465
TITLE: Two Novel and Potent 3-[(o-Methoxyphenyl)piperazinylethyl]-5-phenylthieno[2,3-d]pyrimidine-2,4-diones Selective for the .alpha.1D Receptor
AUTHOR(S): Carroll, W. A.; Sippy, K. B.; Esbenshade, T. A.; Buckner, S. A.; Hancock, A. A.; Meyer, M. D.
CORPORATE SOURCE: Neurological and Urological Diseases Research, Abbott Laboratories, Abbott Park, IL, 60064-6101, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(9), 1119-1121
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



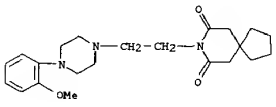
I

AB The synthesis and in vitro characterization of A-119637 (I, R = H) and A-123189 (I, R = Me), two novel, selective and potent .alpha.1D antagonists, are described.
IT 21102-95-4, BMY7378 255893-38-0, SNAP 8719
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(binding to .alpha.1D receptor)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 19 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:207647 CAPLUS
DOCUMENT NUMBER: 134:305637
TITLE: Failure of AH11110A to functionally discriminate between .alpha.1-adrenoceptor subtypes A, B and D or between .alpha.1- and .alpha.2-adrenoceptors
AUTHOR(S): Eltze, M.; Konig, H.; Ullrich, B.; Grebe, T.
CORPORATE SOURCE: Byk Gulden, Department of Pharmacology, Konstanz, D-78467, Germany
SOURCE: European Journal of Pharmacology (2001), 415(2,3), 265-276
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potency of the putatively .alpha.1B-adrenoceptor selective drug, 1-(biphenyl-2-yloxy)-4-imino-4-piperidin-1-yl-butan-2-ol (AH11110A), to antagonize contraction upon stimulation of .alpha.1A-adrenoceptors in rat vas deferens and rat perfused kidney, .alpha.1B-adrenoceptors in guinea-pig spleen, mouse spleen and rabbit aorta, and .alpha.1D-adrenoceptors in rat aorta and pulmonary artery was evaluated and compared to that of a no. of subtype-discriminating antagonists.

N-[3-[4-(2-Methoxyphenyl)-1-piperazinyl]propyl]-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carboxamide (Rec 15/2739) and (.+-.)-1,3,5-trimethyl-6-[[3-[4-((2,3-dihydro-2-hydroxymethyl)-1,4-benzodioxin-5-yl)-1-piperazinyl]propyl]amino]-2,4(1H,3H)-pyrimidinedione (B8805-033) were confirmed as selective for .alpha.1A-adrenoceptors, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]decane-7,9-dione (BMY 7378), 8-[2-(1,4-benzodioxan-2-ylmethylamino)ethyl]-8-azaspiro[4.5]decane-7,9-dione (MDL 73005EF), and cystazosin were found to be selective for .alpha.1D-adrenoceptors, whereas spiperone was weakly selective for .alpha.1B-over .alpha.1A-adrenoceptors. However, from the functional affinity profile obtained for AH11110A at .alpha.1A-adrenoceptors (pA2=6.41 in rat vas deferens), .alpha.1B-adrenoceptors (pA2=5.40-6.54) and .alpha.1D-adrenoceptors (pA2=5.47-5.48), the affinity and presumed selectivity previously obtained for AH11110A in radioligand binding studies at native .alpha.1B- and cloned .alpha.1b-adrenoceptors (pKi=7.10-7.73) could not be confirmed. Addnl., AH11110A enhanced the general contractility of rat vas deferens, produced a bell-shaped dose-response curve of vasodilation in perfused rat kidney, and its antagonism in most other tissues was not simply competitive. The affinity of AH11110A for prejunctional .alpha.2-adrenoceptors in rabbit vas deferens (pA2=5.44) was not much lower than that displayed for .alpha.1-adrenoceptor subtypes, revealing that AH11110A, besides .alpha.1-adrenoceptors, also interacts with .alpha.2-adrenoceptors, and thus may be unsuitable for .alpha.-adrenoceptor subtype characterization,

L14 ANSWER 19 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
at least in smooth muscle contg. functional studies.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(failure of AH11110A to functionally discriminate between .alpha.1-adrenoceptor subtypes A, B and D or between .alpha.1- and .alpha.2-adrenoceptors in animal tissues as compared with other agents)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

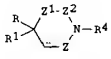
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:63974 CAPLUS
DOCUMENT NUMBER: 134:115867
TITLE: Preparation of azaspirodecane(di)ones and analogs as .alpha.1D adrenoceptor antagonists
INVENTOR(S): Leonardi, Amedeo; Barlocco, Daniela; Motta, Gianni; Testa, Rodolfo
PATENT ASSIGNEE(S): Recordati Industria Chimica e Farmaceutica S.p.A., Italy; Recordati S.A., Chemical and Pharmaceutical Company
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

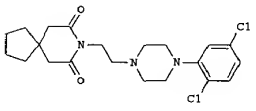
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005765	A1	20010125	WO 2000-EP6738	20000714
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 99MI1578	A1	20010115	IT 1999-MI1578	19990715
EP 1200456	A1	20020502	EP 2000-945917	20000714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: IT 1999-MI1578 A 19990715
WO 2000-EP6738 W 20000714
OTHER SOURCE(S): MARPAT 134:115867
GI

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



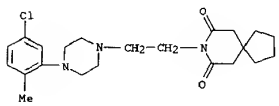
I



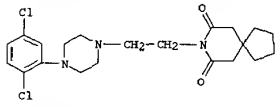
II

AB Title compds. [I; R,R1 = H or alkyl; RR1 = (CH2)2-6; R4 = CHR3CHR7CHR3; R3 = H or alkyl; R7 = Z3Z4R2; R2 = halo, alkyl, cyano; Z = CH2, CO, CH; Z1 = bond or CH2; Z2 = CH2 or CO; Z3 = piperidine- or -azine-1,4-diyl or NMe(CH2)mZ5Z4R2; Z4 = (un)substituted 1,2-phenylene; Z5 = O, S, NH, NMe; m = 2-4; dashed line = optional addnl. bond] were prepd. Thus, 8-(2-bromoethyl)-8-azaspiro[4.5]decane-7,9-dione was aminated by 1-(2,5-dichlorophenyl)piperazine to give title compd. II. Data for biol. activity of I were given.
IT **255893-42-6P 321601-67-5P 321601-68-7P**
321601-69-8P 321601-70-1P 321601-71-2P
321601-72-3P 321601-73-4P 321601-74-5P
321601-75-6P 321601-76-7P 321601-77-8P
321601-78-9P 321601-79-0P 321601-80-3P
321601-81-4P 321601-82-5P 321601-83-6P
321601-84-7P 321601-87-0P 321601-89-2P
321601-90-5P 321601-91-6P 321601-92-7P
321601-93-8P 321601-94-9P 321601-95-0P
321601-96-1P 321601-97-2P 321602-28-2P
321602-36-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azaspirodecane(di)ones and analogs as .alpha.1D adrenoceptor antagonists)
RN 255893-42-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



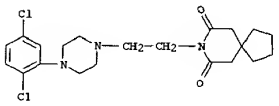
RN 321601-67-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 321601-68-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 321601-67-6
CMF C21 H27 Cl2 N3 O2



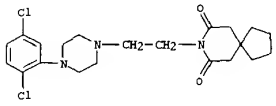
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 321601-69-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, dimethanesulfonate (9CI) (CA INDEX NAME)

CM 1

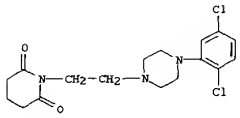
CRN 321601-67-6
CMF C21 H27 Cl2 N3 O2



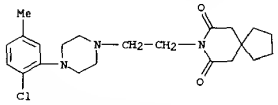
CM 2

CRN 75-75-2
CMF C H4 O3 S

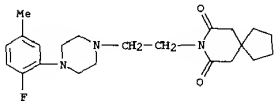
RN 321601-70-1 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



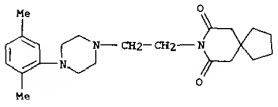
RN 321601-71-2 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



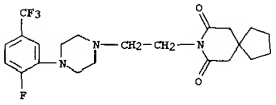
RN 321601-72-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-fluoro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



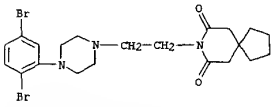
RN 321601-73-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



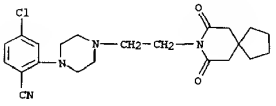
RN 321601-74-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-[2-fluoro-5-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



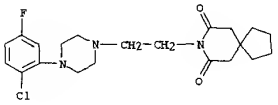
RN 321601-75-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dibromophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



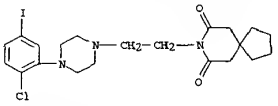
RN 321601-76-7 CAPLUS
CN Benzonitrile, 4-chloro-2-[4-[2-(7,9-dioxo-8-azaspiro[4.5]dec-8-yl)ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



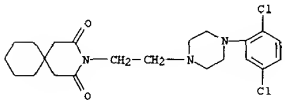
RN 321601-77-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



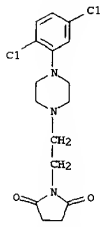
RN 321601-78-9 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-iodophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



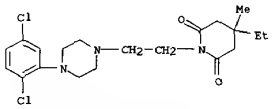
RN 321601-79-0 CAPLUS
CN 3-Azaspiro[5.5]undecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



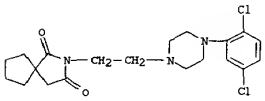
RN 321601-80-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 321601-81-4 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-4-ethyl-4-methyl- (9CI) (CA INDEX NAME)

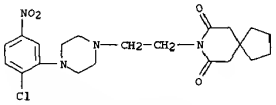


RN 321601-82-5 CAPLUS
CN 2-Azaspiro[4.4]nonane-1,3-dione, 2-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

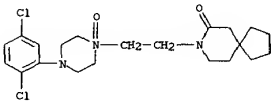


RN 321601-83-6 CAPLUS
CN 7-Azaspiro[3.5]nonane-6,8-dione, 7-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

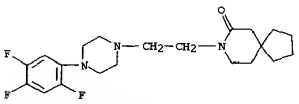
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-nitrophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



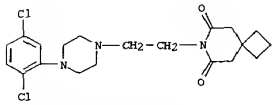
RN 321601-91-6 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-oxido-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



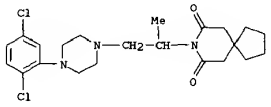
RN 321601-92-7 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



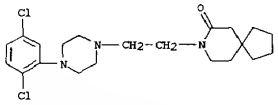
RN 321601-93-8 CAPLUS
CN 3-Azaspiro[5.5]undecan-2-one, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



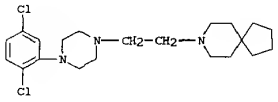
RN 321601-84-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



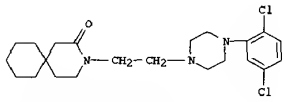
RN 321601-87-0 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



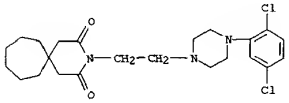
RN 321601-89-2 CAPLUS
CN 8-Azaspiro[4.5]decane, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



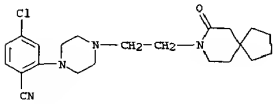
RN 321601-90-5 CAPLUS



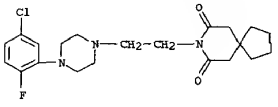
RN 321601-94-9 CAPLUS
CN 3-Azaspiro[5.6]dodecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



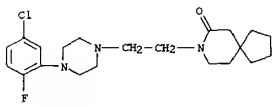
RN 321601-95-0 CAPLUS
CN Benzonitrile, 4-chloro-2-[4-[2-(7-oxo-8-azaspiro[4.5]dec-8-yl)ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



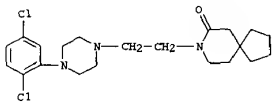
RN 321601-96-1 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 321601-97-2 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

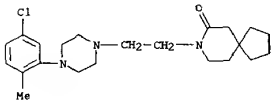


RN 321602-28-2 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



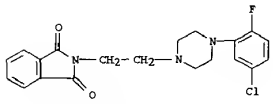
● HCl

RN 321602-36-2 CAPLUS
CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

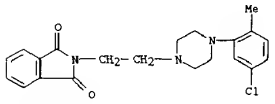


IT **321602-22-6P 321602-24-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of azaspirodecane(di)ones and analogs as .alpha.1D adrenoceptor
antagonists)

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 321602-22-6 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

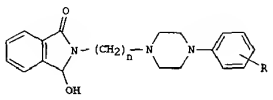


RN 321602-24-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



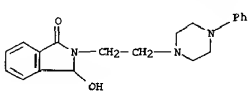
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:780228 CAPLUS
DOCUMENT NUMBER: 134:71569
TITLE: Preparation of N-[.omega.-(4-aryl-1-piperazinyl)ethyl/propyl]-3-hydroxyphthalimidines
AUTHOR(S): Desai, R. A.; Samant, S. D.
CORPORATE SOURCE: Organic Chemistry Research Laboratory, University Department of Chemical Technology, Mumbai, 400 019, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2000), 39B(6), 455-457
CODEN: IJSBDB; ISSN: 0376-4699
PUBLISHER: National Institute of Science Communication, CSIR
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:71569
GI

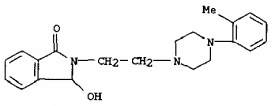


I

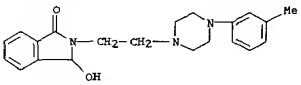
AB The reaction of .omega.-(4-aryl-1-piperazinyl)ethyl/propyl amine with 3-hydroxyphthalide furnishes the title compds. I (n = 2, 3; R = H, 2-, 3-, 4-Me, Cl) along with minor amts. of the corresponding N-[.omega.-(4-aryl-1-piperazinyl)ethyl/propyl]-2-formylbenzamides.
IT **316146-14-2P 316146-15-3P 316146-17-5P 316146-20-0P 316146-22-2P 316146-24-4P 316146-26-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 316146-14-2 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



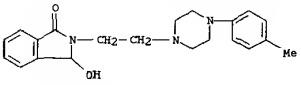
L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 316146-15-3 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



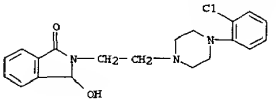
RN 316146-17-5 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



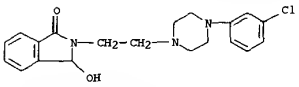
RN 316146-20-0 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



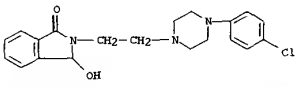
RN 316146-22-2 CAPLUS
CN 1H-Isoindol-1-one, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 316146-24-4 CAPLUS
CN 1H-Isoindol-1-one, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



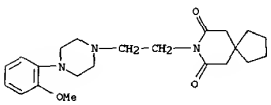
RN 316146-26-6 CAPLUS
CN 1H-Isoindol-1-one, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:779744 CAPLUS
DOCUMENT NUMBER: 134:857
TITLE: An .alpha.1A/.alpha.1L-adrenoceptor mediates contraction of canine subcutaneous resistance arteries
AUTHOR(S): Argyle, Sally Anne; McGrath, John Christie
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical & Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 295(2), 627-633
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. the characteristics of the .alpha.1-adrenoceptor subtypes involved in adrenergic regulation of peripheral vascular resistance, contraction of canine s.c. resistance arteries was studied using wire myographs. The potencies of agonists and antagonists, chosen for their ability to discriminate between .alpha.1-adrenoceptor subtypes, were assessed in the presence of cocaine (3 .mu.M), corticosterone (30 .mu.M), and propranolol (1 .mu.M). The rank order of agonist potency (pEC50 .+-. S.E.) was (R)-A-61603 (7.88.+-.0.1) > norepinephrine (6.41.+-.0.1) > phenylephrine (5.83.+-.0.1). The high sensitivity to (R)-A-61603 relative to phenylephrine is inconsistent with the presence of the .alpha.1D-adrenoceptor and most consistent with an .alpha.1A-adrenoceptor response. This is supported by the low affinity for the .alpha.1D-selective antagonist BMY 7378 (pKB 6.51.+-.0.47). The low pA2 values for prazosin (8.36) and HV723 (8.81), by definition, indicate the involvement of the putative .alpha.1L-adrenoceptor, a hypothesis supported by the pA2 values for WB4101 (8.42) and 5-methyl-urapidil (8.08). Pre-exposure to 1 .mu.M CEC had little effect, whereas 100 .mu.M CEC reduced the max. contraction but not the sensitivity to norepinephrine. This low sensitivity to CEC argues against the presence of the .alpha.1B-adrenoceptor. We conclude that, by current definitions, an .alpha.1A-/.alpha.1L-adrenoceptor causes contraction of these vessels. This does not support the concept that selectivity for the .alpha.1A-adrenoceptor is the basis for the effectiveness of some .alpha.-blockers in some tissues, such as prostate, but not in other tissues such as blood vessels. Rather, the generally low potency of .alpha.-blockers in some tissues may be due to a tissue-specific property

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
of the receptors.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1A/.alpha.1L-adrenoceptor mediates contraction of canine s.c. resistance arteries)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

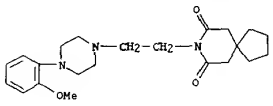


●2 HCl

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:757753 CAPLUS
DOCUMENT NUMBER: 134:51220
TITLE: Pharmacological characterization of [3H]-JTH-601, a novel .alpha.1-adrenoceptor antagonist binding to recombinant human .alpha.1-adrenoceptors and human prostates
AUTHOR(S): Takahashi, Masahiko; Taniguchi, Takanobu; Kanamaru, Hiroshi; Okada, Kenichiro; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: Life Sciences (2000), 67(20), 2443-2451
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several .alpha.1-adrenoceptor (AR) selective antagonists are now widely used to improve lower urinary tract symptoms in benign prostatic hyperplasia patients. However, these drugs often result in orthostatic hypotension, because of their poor uroselectivity; the blockade of .alpha.1-AR not only in prostate but also in vasculature. Here we have investigated uroselectivity of JTH-601, a newly developed antagonist, in radioligand binding expt. using recombinant human .alpha.1-AR subtypes and human prostate. In satn. expts., [3H]-JTH-601 showed subtype selectivity: high affinity to .alpha.1a-AR (pKd; 9.88.+-.0.09), lower affinity to .alpha.1b-AR (pKd; 8.96.+-.0.17) and no specific binding at concns. up to 3000 pM to .alpha.1d-AR. In competition expts., JTH-601 and its metabolic compd. (JTH-601-G1) also showed .alpha.1a-AR selectivity, exhibiting approx. 5 times higher affinity for .alpha.1a-AR than for .alpha.1b-AR, 10 to 20 times higher affinity than for .alpha.1d-AR, resp. [3H]-JTH-601 also bound to human prostate membranes in monophasic manner with high affinity const. (pKd; 9.89.+-.0.12, Bmax=123.6.+-.16 fmol/mg protein). JTH-601 is a unique .alpha.1-AR antagonist that shows high affinity and selectivity for human recombinant .alpha.1a- and human prostate. This new compd. is useful for understanding .alpha.1-AR pharmacol. and may have a therapeutic value.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(pharmacol. characterization of [3H]-JTH-601, a novel .alpha.1-adrenoceptor antagonist binding to recombinant human .alpha.1-adrenoceptors and human prostates)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

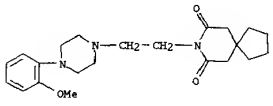


●2 HCl

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:719190 CAPLUS
DOCUMENT NUMBER: 133:344153
TITLE: Development of scintillation-proximity assays for alpha adrenoceptors
AUTHOR(S): Gobel, J.; Saussy, D. L.; Goetz, A. S.
CORPORATE SOURCE: Department of Receptor Biochemistry, Glaxo Wellcome
Research and Development, Research Triangle Park, NC,
27709, USA
SOURCE: Journal of Pharmacological and Toxicological Methods
(1999), 42(4), 237-244
CODEN: JPTMEZ; ISSN: 1056-8719
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding assays have long been used to det. compd. affinity and selectivity for various seven-transmembrane receptors. Over time, the degree of complexity has significantly reduced, whereas the throughput of the various assays has greatly increased. In this article, the authors detail the development of a filter-binding assay and a scintillation-proximity assay (SPA) designed to quantify a compd.'s affinity for the three .alpha.1-adrenoceptor subtypes, .alpha.1A, .alpha.1B, and .alpha.1D. The various components of the assays such as ease of assay performance, robustness, cost, and generation of radioactive waste are compared and contrasted. On the basis of the results, the SPA offers many advantages of high-throughput assay formats over the traditional filter-binding assay. To follow up on the success of the .alpha.1-adrenoceptor SPA, SPAs for the three .alpha.2-adrenoceptors were developed and are detailed in this article. Affinity data generated for a select no. of .alpha.2 compds. agree with reported literature values. These assays, like those for .alpha.1 subtypes, are very amenable to high-throughput screening campaigns. In conclusion, scintillation-proximity assays offer significant advantages over filter-binding assays.
IT **21102-95-4**, BMY 7378
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(scintillation-proximity assays to quantify compd.'s affinity for alpha adrenoceptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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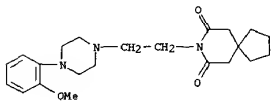
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:667305 CAPLUS
DOCUMENT NUMBER: 133:359442
TITLE: .alpha.1-Adrenoceptors in the guinea pig thoracic aorta
AUTHOR(S): Yamamoto, Yoshihisa; Koike, Katsuo
CORPORATE SOURCE: Department of Chemical Pharmacology, Toho University
School of Pharmaceutical Sciences, Chiba, 274-8510,
Japan
SOURCE: Journal of Smooth Muscle Research (1999), 35(5,6), 181-192
CODEN: JSMRE2; ISSN: 0916-8737
PUBLISHER: Japanese Society of Smooth Muscle Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present study, the authors tried to det. which .alpha.1-adrenoceptor subtypes are involved in the guinea pig thoracic aorta by using in vitro functional anal. Firstly, the authors tried to est. the pA2 values of some key .alpha.1-adrenoceptor antagonists (prazosin, 5-methylurapidil, WB4101, BMY7378 and tamsulosin) against responses to norepinephrine in the thoracic aorta of guinea pigs. The concn.-response curves of norepinephrine were rightward shifted by the presence of prazosin, 5-methylurapidil, WB4101, BMY7378 and tamsulosin. The pA2 values for these antagonists against norepinephrine were 7.83, 7.78, 8.20, 5.73 and 9.57, resp. Secondly, the authors tried to compare the estd. pA2 values obtained in the present study with reported pKi and pA2 values for cloned and native .alpha.1-adrenoceptor subtypes. In rabbit mesenteric artery, trigone, urethra, prostate and human lower urinary tract which were proposed to contain the putative .alpha.1L-adrenoceptor, the authors obtained a good correlation for the pA2 values reported in these tissues with pA2 values estd. in guinea pig thoracic aorta. Moreover, regression lines were close to the line of identity. These results suggest that the .alpha.1-adrenoceptors mediating contraction of guinea pig thoracic aorta are similar pharmacol. to the putative .alpha.1L-adrenoceptor subtype in rabbit mesenteric artery, trigone, urethra, prostate and human lower urinary tract. As a final point, guinea pig thoracic aorta may be used as a tool to develop new .alpha.1-adrenoceptor antagonists therapeutically advantageous in the treatment of urinary tract obstruction (e.g., in benign prostatic hyperplasia).
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

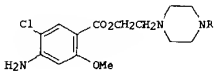
L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor antagonist; .alpha.1-adrenoceptor subtypes mediating vasoconstriction in guinea pig thoracic aorta)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

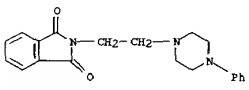
L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:653172 CAPLUS
DOCUMENT NUMBER: 133:362752
TITLE: New Arylpiperazine Derivatives as Antagonists of the Human Cloned 5-HT4 Receptor Isoforms
AUTHOR(S): Curtet, Sophie; Soulier, Jean-Louis; Zahradnik, Ivan; Giner, Mireille; Berque-Bestel, Isabelle; Mialet, Jeanne; Lezoualc'h, Frank; Donzeau-Gouge, Patrick; Sicsic, Sames; Fischmeister, Rodolphe; Langlois, Michel
CORPORATE SOURCE: INSERM U-446 Institut de Signalisation et Innovation Therapeutique (IFR-ISIT) Faculte de Pharmacie, CNRS-BIOCIS (UPRES A 8076) and Laboratoire de Cardiologie Cellulaire et Moleculaire Universite de Paris-Sud, Chatenay-Malabry, 92296, Fr.
SOURCE: Journal of Medicinal Chemistry (2000), 43(20), 3761-3769
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:362752
GI



I

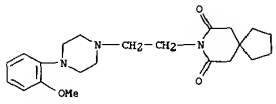
AB New derivs. of arylpiperazine I [R = (un)substituted Ph, 1-naphthyl, CO2Et, CO2CMe3, Me, H, pyrimidinyl, pyrazinyl, pyridazinyl, pyridinyl] were designed from ML 10302, a potent 5-HT4 receptor agonist in the gastrointestinal system. I were synthesized by condensation of the arylpiperazines or heteroarylpiperazines with 2-bromoethyl 4-amino-5-chloro-2-methoxybenzoate. I were evaluated in binding assays on the recently cloned human 5-HT4(e) isoform stably expressed in C6 glial cells with [3H]GR 113808 as the radioligand. The affinity values (Ki) depended upon the substituent on the arom. ring. A chlorine atom produced a marked drop in activity (Ki > 100 nM), while a m-methoxy group gave a compd. with nanomolar affinity (Ki = 3 nM). The most potent compds. were the heterocyclic derivs. with pyrimidine, pyrazine, pyridazine, or pyridine moieties. Ki values for I [R = Ph, 2-pyrimidinyl] were detd. for

L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
the 5-HT4(a), 5-HT4(b), 5-HT4(c), and 5-HT4(d) receptor isoforms transiently expressed in COS cells. The results indicated that the compds. were not selective. They produced an inhibition of the 5-HT-stimulated cAMP synthesis in the C6 glial cells stably expressing the 5-HT4(e) receptor and shifted the 5-HT concn.-effect curve on adenylyl cyclase activity with pKD values of 7.44 and 8.47, resp. In isolated human atrial myocytes, I [R = 2-pyrimidinyl] antagonized the stimulatory effect of 5-HT on the L-type calcium current (ICa) with a KD value of 0.7 nM.
IT **75000-24-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(arylpiperazinylethyl aminobenzoates as antagonists of the human cloned 5-HT4 receptor isoforms)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
(CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:565500 CAPLUS
DOCUMENT NUMBER: 134:25262
TITLE: Effects of the 5HT1A agonist/antagonist BMY 7378 on light-induced phase advances in hamster circadian activity rhythms during aging
AUTHOR(S): Byku, Mirnela; Gannon, Robert L.
CORPORATE SOURCE: Department of Biology, Dowling College, Oakdale, NY, 11769, USA
SOURCE: Journal of Biological Rhythms (2000), 15(4), 300-305
CODEN: JBRHEE; ISSN: 0748-7304
PUBLISHER: Sage Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BMY 7378 was a highly effective chronobiotic that more than doubled the magnitude of light-induced phase shifts in hamster wheel-running activity rhythms. Light-induced phase advances of .gtoreq.6 h in hamster wheel-running activity following a single systemic dose of BMY 7378 were obsd. Furthermore, the BMY 7378 potentiation of phase shifts was maintained in old hamsters, suggesting that BMY 7378 has a different site of activity than that of previously reported 5HT1A agonists that have a diminished effect on circadian phase during aging.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serotoninergic1A agonist/antagonist BMY 7378 effect on light-induced phase advances in circadian activity during aging)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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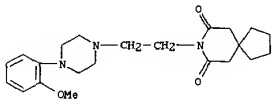
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:558944 CAPLUS
DOCUMENT NUMBER: 133:276210
TITLE: Tissue selectivity of KMD-3213, an .alpha.1-adrenoceptor antagonist, in human prostate
and vasculature
AUTHOR(S): Murata, Satoshi; Taniguchi, Takanobu; Takahashi, Masahiko; Okada, Kenichiro; Akiyama, Katsuyoshi; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology and Urology, School of Medicine, Fukui Medical University, Matsuoka, Japan
SOURCE: Journal of Urology (Baltimore) (2000), 164(2), 578-583
CODEN: JDURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We evaluated the binding and functional affinity of KMD-3213 and other .alpha.1-adrenoceptor (AR) antagonists such as prazosin or tamsulosin, to compare the tissue selectivity of these antagonists between human prostate and vasculature. In the binding expts., satn. expts. using [3H]-KMD and [3H]-prazosin (PZ) were performed, and competition of [3H]-PZ binding by antagonists was also examd. in human prostatic and aortic membranes. In the functional study, contractile responses to noradrenaline were evaluated in human prostate and mesenteric artery. [3H]-PZ bound to human prostatic and aortic membranes with subnanomolar affinity. [3H]-KMD also bound to human prostate, with higher affinity than [3H]-PZ; whereas it did not bind sufficiently to human aorta. Competition of [3H]-PZ binding revealed that KMD-3213 had more than 200-fold higher affinity for human prostate than for aorta. Binding profiles of antagonists revealed that human prostate predominantly expressed .alpha.1A-AR, whereas human aorta expressed .alpha.1B-AR mainly. In functional expts., KMD-3213 potently inhibited the noradrenaline-induced contraction in human prostate as potently as tamsulosin, although prazosin showed relatively low affinity. Comparing these functional affinities with those in the mesenteric artery, only KMD-3213 exhibited substantial tissue selectivity, showing more than 100-fold higher affinity for human prostate than for mesenteric artery. Functional affinity of each antagonist suggested that noradrenaline-induced contractions were mainly mediated by .alpha.1L-AR in the human

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
prostate and by .alpha.1B-AR in the mesenteric artery. These results suggest that KMD-3213 is a substantially prostate-selective .alpha.1-AR antagonist in human tissues compared with other .alpha.1-AR antagonists.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tissue selectivity of KMD-3213 and other .alpha.1-adrenoceptor antagonists in human prostate and vasculature)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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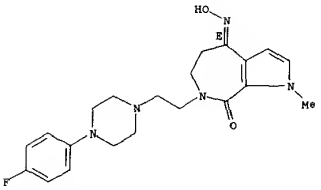
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 29 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:554947 CAPLUS
DOCUMENT NUMBER: 133:281710
TITLE: Studies on antihypertensive agents with antithrombotic activity. 2. Syntheses and pharmacological evaluation of pyrrolo[2,3-c]azepine derivatives
AUTHOR(S): Mizuno, Akira; Miya, Mikiko; Kamei, Tomoe; Shibata, Makoto; Tatsuoka, Toshio; Nakanishi, Kyoko; Takiguchi, Chikako; Hidaka, Toshinori; Yamaki, Akira; Inomata, Norio
CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka, 618-8503, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(8), 1129-1137
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 7-aminoalkylpyrrolo[2,3-c]azepine derivs. was synthesized and evaluated as .alpha.1-adrenergic and 5-HT2 receptor antagonists, with the aim of finding a novel potent antihypertensive agent with both activities. Among the compds. obtained in this study, (E)-1-ethyl-7-[3-[4-(4-fluorophenyl)piperazin-1-yl]propyl]-4-hydroxyimino-1,4,5,6,7,8-hexahydropyrrolo[2,3-c]azepin-8-one (1) displayed potent .alpha.1-adrenoceptor blocking activity (pA2 = 7.83 .+-. 0.20) and 5-HT2-receptor blocking activity (pA2 = 9.47 .+-. 0.17) in isolated guinea pig arteries. At 3 mg/kg oral administration, I exhibited antihypertensive activity more potent than that of doxazosin in deoxycorticosterone acetate (DOCA)-salt hypertensive dogs. Furthermore, this compd. reduced the rate of mouse acute pulmonary thromboembolitic death induced by collagen and serotonin at oral doses of 0.3 mg/kg or more, and its effect lasted for at least 6 h at 3 mg/kg.
IT **300548-34-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of aminoalkylpyrroloazepinediones with .alpha.-adrenergic and 5-HT2 antagonist activity)
RN 300548-34-9 CAPLUS
CN Pyrrolo[2,3-c]azepine-4,8(1H,5H)-dione, 7-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl-, 4-oxime, (4E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

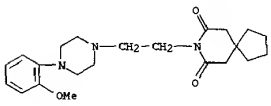
L14 ANSWER 29 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:536311 CAPLUS
DOCUMENT NUMBER: 134:157934
TITLE: Quantitative imaging in live human cells reveals intracellular .alpha.1-adrenoceptor ligand-binding sites
AUTHOR(S): Mackenzie, Janet F.; Daly, Craig J.; Pediani, John D.; McGrath, John C.
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical & Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 294(2), 434-443
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cellular distribution and binding characteristics of native .alpha.1-adrenoceptors (ARs) were detd. in a live, single, human smooth muscle cell (SMC) with confocal laser scanning microscopy and a fluorescent ligand, BODIPY-FL prazosin (QAPB). This allowed single-cell competitive ligand binding and showed that 40% of .alpha.1-AR-binding sites in native cells are intracellular. QAPB had high affinity and acted as a nonselective, competitive antagonist vs. [3H]prazosin at cloned human .alpha.1a-, .alpha.1b-, and .alpha.1d-AR subtypes on membrane prepns. and whole cells. RS100329 had 70-fold selectivity for .alpha.1a-ARs vs. .alpha.1b- and .alpha.1d-ARs, validating its use to identify this subtype. In similar cells QAPB-assocd. fluorescence provided quant. data analogous and comparable to [3H]prazosin binding in whole cells. In human, dissocd., prostatic smooth muscle cells QAPB-assocd. fluorescence binding exhibited specific high-affinity binding properties (FKD = 0.63.+-.0.02 nM), which was 3- to 4-fold higher compared with recombinant cells (FKD = 2.1-2.3 nM). Internal consistency in the data showed that affinity is greater, in general, in membrane prepns. than in cells but also greater in the native prostatic tissues or cells than in equiv. recombinant receptors. Fluorescence revealed binding sites both on the plasmalemmal membrane and on intracellular compartments: at all locations RS100329 inhibited QAPB binding identifying the sites as .alpha.1A-ARs. Quant. three-dimensional mapping of QAPB-assocd. fluorescence binding in native

L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
human cells showed that 40% of high-affinity-binding sites was in intracellular compartments. This provides a potential new site for physiol. agonism and makes intracellular access a potential differentiator of drug action.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor ligand-binding sites are intracellularly localized in live human prostatic smooth muscle cells)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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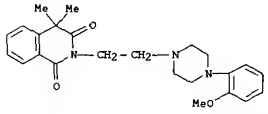
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:458289 CAPLUS
DOCUMENT NUMBER: 133:130140
TITLE: Characterization of the .alpha.2-adrenoceptor subtype, which functions as .alpha.2-autoreceptor in human neocortex
AUTHOR(S): Feuerstein, Thomas J.; Huber, Boris; Vetter, Jan; Aranda, Heike; Van Velthoven, Vera; Limberger, Norbert
CORPORATE SOURCE: Sektion Klinische Neuropharmakologie der Neurologischen Universitatsklinik, Freiburg, D-79106, Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 294(1), 356-362
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacol. properties of the .alpha.2-adrenergic receptors regulating the release of norepinephrine were investigated in human neocortex. Slices were preincubated with [3H]norepinephrine, superfused under blockade of transmitter reuptake, and stimulated elec. First, the autoinhibitory circuit of [3H]norepinephrine release was analyzed quant. by estn. of the Kd of norepinephrine at the .alpha.2-autoreceptor (10-7.99 M), the concn. of the endogenous transmitter causing this autoinhibition at a stimulation frequency of 3 Hz (10-7.61 M), and the max. inhibition obtainable through the autoreceptor (83%). Second, antagonist pKb values of nine antagonists were detd. by using their pEC50 values (neg. logarithms of antagonist concns. that increased the elec. evoked overflow of tritium by 50%) against the release-inhibiting effect of the endogenous transmitter. When compared with binding or functional data from the literature, the pKb values correlated best with the antagonist affinities at .alpha.2A binding sites. In contrast, the correlations with .alpha.2B, .alpha.2C, and .alpha.2D sites were not as good. It is concluded that in human neocortex prejunctional autoreceptors are .alpha.2A.
IT **67339-62-2**, ARC239
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(norepinephrine release from human neocortex and calcn. of unbiased

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
dissocn. consts. of antagonists in relation to characterization of .alpha.2-adrenoceptor subtype which functions as .alpha.2-autoreceptor
in human neocortex)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:455295 CAPLUS
DOCUMENT NUMBER: 133:89543
TITLE: Preparation of 1-[3-(2,5-dioxopyrrolidino- or 2,6-dioxopiperidino)propyl]-4-arylpiperazines and analogs as uroselective .alpha.1-adrenoceptor antagonists
INVENTOR(S): Anand, Nitya; Sinha, Neelima; Jain, Sanjay; Mehta, Anita; Bahadurgupta, Jang
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6083950	A	20000704	US 1998-120265	19980721
US 6090809	A	20000718	US 1998-203855	19981202
WO 2000005206	A1	20000203	WO 1999-IB140	19990126

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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9919797	A1	20000214	AU 1999-19797	19990126
WO 2000005205	A1	20000203	WO 1999-IB1296	19990716

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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AU 9946410	A1	20000214	AU 1999-46410	19990716

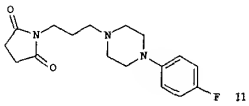
L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

BR 9912318	A	20010502	BR 1999-12318	19990716
EP 1097134	A1	20010509	EP 1999-929633	19990716

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

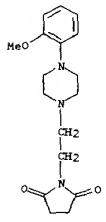
US 6410735	B1	20020625	US 2000-578088	20000524
US 6420366	B1	20020716	US 2000-577788	20000524
US 6420559	B1	20020716	US 2000-577789	20000524

PRIORITY APPLN. INFO.:
IN 1997-DE3260 A 19971113
IN 1997-DE3261 A 19971113
US 1998-120265 A3 19980721
WO 1999-IB140 W 19990126
WO 1999-IB1296 W 19990716
OTHER SOURCE(S): MARPAT 133:89543
GI



AB Title compds., e.g., R(CH2)nCHR3CH2R1 [I; R = 2,5-dioxopyrrolidino, 2,6-dioxopiperidino, etc.; R1 = (un)substituted 2-pyridinyl, -2-pyrimidinyl, -Ph; R3 = H, OH, alkyl, alkoxy; Z = piperidine- or piperazine-1,4-diyl; n = 0-4] were prepd. Thus, 2,5-dioxopyrrolidine was
N-alkylated by 1-(3-chloropropyl)-4-(4-fluorophenyl)piperazine to give
title compd. II. Data for biol. activity of I were given.
IT **255861-61-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-[3-(2,5-dioxopyrrolidino- or 2,6-dioxopiperidino)propyl]-4-
arylpiperazines and analogs as uroselective .alpha.1-adrenoceptor antagonists)
RN 255861-61-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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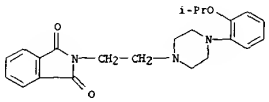
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

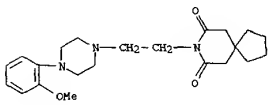
L14 ANSWER 33 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:379674 CAPLUS
DOCUMENT NUMBER: 133:150523
TITLE: Novel arylpiperazines as selective .alpha.1-adrenergic receptor antagonists
AUTHOR(S): Li, Xiaobing; Murray, William V.; Jolliffe, Linda; Pulito, Virginia
CORPORATE SOURCE: The R. W. Johnson Pharmaceutical Research Institute, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(10), 1093-1096
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel series of arylpiperazines has been synthesized and identified as antagonists of .alpha.1a adrenergic receptor (.alpha.1a-AR) implicated in benign prostatic hyperplasia. These compds. selectively bind to membrane bound .alpha.1a-AR with Kis as low as 0.66 nM. As such, these potentially represent a viable treatment for BPH without the side effects assocd. with known .alpha.1-adrenergic antagonists.
IT **216252-67-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of arylpiperazines as selective .alpha.1-adrenergic receptor antagonists)
RN 216252-67-4 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[2-(1-methylethoxy)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 34 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:373728 CAPLUS
DOCUMENT NUMBER: 133:84624
TITLE: Single-cell recombinant pharmacology: bovine .alpha.1a-adrenoceptors in rat-1 fibroblasts release intracellular Ca2+, display subtype-characteristic agonism and antagonism, and exhibit an antagonist-reversible inverse concentration-response phase
AUTHOR(S): Pediani, John Daniel; Mackenzie, Janet Fraser; Heeley, Robert Paul; Daly, Craig James; Mcgrath, John Christie
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 887-895
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phenylephrine (Phe)-activated Ca2+ signals recorded from single rat-1 fibroblasts stably expressing the bovine .alpha.1a-adrenoceptor (AR) were characterized and used to analyze functional agonist-antagonist interactions. The response to Phe was initiated by the mobilization of stored Ca2+ and subsequently sustained by receptor-regulated Ca2+ influx.
The selective .alpha.1A-AR agonist (R)-A-61603 was 141-fold more potent as an agonist than Phe. This potency ratio was consistent with the pharmacol. of the native .alpha.1A-ARs. Functional responses evoked by concns. of Phe of more than 0.3 .mu.M displayed fade, which could be explained by agonist-dependent depletion of Ca2+ stores. The antagonists tested did not conform to the predictions of the Schild equation for competitive antagonism as expected from the nonequil. nature of the response. The antagonist potency series WB 4101 .gtoreq. prazosin .mchgt. BMY 7378, however, was consistent with .alpha.1A-ARs. Antagonism exhibited by WB 4101 and prazosin was compatible with a model in which antagonists dissoc. so slowly from the receptor that this is a major factor in their inhibition of the transient agonist-mediated response, leading to the appearance of insurmountable antagonism. A consequence of this phenomenon was that an inverse concn.-response relationship at high agonist concns. was abolished by low concns. of antagonists. Overall, the

L14 ANSWER 34 OF 263 CAPLUS (Continued)
results indicate that quant. pharmacol. can be studied successfully in single cells even though equil. could not be achieved in the agonist-antagonist-response relationship in this particular cell phenotype. The study also showed a form of fade that could be readily explained.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(single-cell recombinant pharmacol. of bovine .alpha.1a-adrenoceptor in rat-1 fibroblasts and intracellular calcium release)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



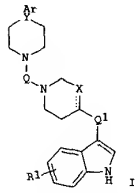
●2 HCl

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:345474 CAPLUS
DOCUMENT NUMBER: 132:347587
TITLE: Preparation of piperazinylalkylpiperidinyl(alkyl)indoles as serotonergic agents.
INVENTOR(S): Kelly, Michael G.; Kang, Young H.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6066637	A	20000523	US 1999-298202	19990423

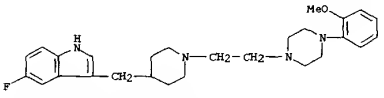
PRIORITY APPLN. INFO.: US 1998-100433P P 19980429
OTHER SOURCE(S): MARPAT 132:347587
GI



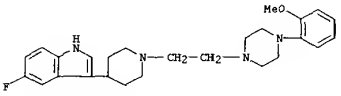
AB Title compds. [I; R1 = H, OH, OR2, F, Cl, Br, iodo; R2 = alkyl; Q = (CH2)m; Q1 = (CH2)n; n = 0-2; X = CH, CH2; m = 2-4; Y = N, CH2; Ar = (substituted) aryl, heteroaryl], were prepd. Thus, 4-(5-fluoro-1H-indol-3-ylmethyl)piperidine, 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine, and K2CO3 were refluxed 5 h in MeCN to give 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]piperidin-4-ylmethyl]-1H-indole. I displaced [3H]-paroxetine from serotonin transporters with Ki = 1.2-19 nM.
IT **247911-01-9P 247911-02-0P 247911-05-3P**
247911-06-4P 247911-07-5P 247911-08-6P
247911-09-7P 247911-12-2P 247911-14-4P
247911-15-5P 247911-16-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazinylalkylpiperidinyl(alkyl)indoles as serotonergic agents)

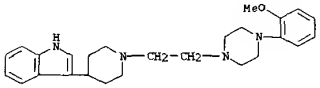
RN 247911-01-9 CAPLUS
CN 1H-Indole, 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 247911-02-0 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)

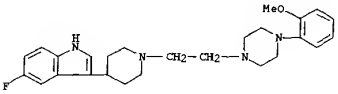


RN 247911-05-3 CAPLUS
CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 247911-06-4 CAPLUS
CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

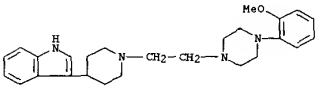


●2 HCl

RN 247911-12-2 CAPLUS
CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

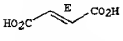
CRN 247911-05-3
CMF C26 H34 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

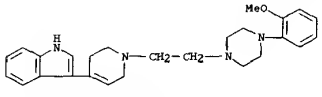


RN 247911-14-4 CAPLUS
CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

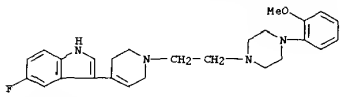
CM 1

CRN 247911-06-4
CMF C26 H32 N4 O

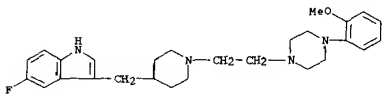
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 247911-07-5 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



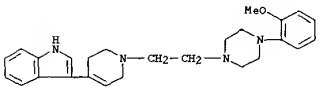
RN 247911-08-6 CAPLUS
CN 1H-Indole, 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 247911-09-7 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

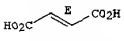
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

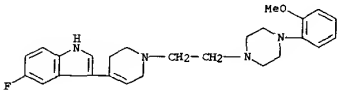
Double bond geometry as shown.



RN 247911-15-5 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

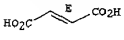
CRN 247911-07-5
CMF C26 H31 F N4 O



CM 2

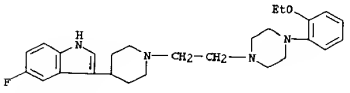
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

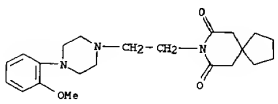
RN 247911-16-6 CAPLUS
CN 1H-Indole, 3-[1-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-5-fluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:345446 CAPLUS
DOCUMENT NUMBER: 133:99703
TITLE: Cloning of rabbit .alpha.1b-adrenoceptor and pharmacological comparison of .alpha.1a-, .alpha.1b- and .alpha.1d-adrenoceptors in rabbit
AUTHOR(S): Piao, H.; Taniguchi, T.; Nakamura, S.; Zhu, J.; Suzuki, F.; Makami, D.; Muramatsu, I.
CORPORATE SOURCE: School of Medicine, Department of Pharmacology, Fukui Medical University, Matsuoka, Fukui, 910-1193, Japan
SOURCE: European Journal of Pharmacology (2000), 396(1), 9-17
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have isolated a cDNA clone of the rabbit .alpha.1b-adrenoceptor which has an open reading frame of 1557 nucleotides encoding a protein of 518 amino acids. The sequence shows higher identity to those of hamster, human, and rat .alpha.1b-adrenoceptors than to those of rabbit .alpha.1a- and .alpha.1d-adrenoceptors. The pharmacol. binding properties of this clone expressed in Cos-7 cells showed a characteristic profile as .alpha.1b-adrenoceptor; high affinity for prazosin (pKi=10.3), relatively high affinity for tamsulosin (9.5) and low affinity for KMD 3213 (8.5), WB 4101 (8.7), and BMY 7378 (7.3). We have compared the levels of mRNA expression of three .alpha.1-adrenoceptor subtypes in rabbit tissues using the competitive reverse transcription/polymerase chain reaction (RT/PCR) assay. In most rabbit tissues except heart, .alpha.1a-adrenoceptor mRNA was expressed 10 folds more than the other two subtypes. However, binding expts. with [3H]prazosin and [3H]KMD 3213 in rabbit tissues revealed a poor relationship between binding d. and mRNA level. Esp., .alpha.1b binding sites were exclusively predominant in spleen, whereas the .alpha.1b subtype was minor at the mRNA level. These results indicate a high identity of structural and pharmacol. profiles of three distinct .alpha.1-adrenoceptor subtypes between rabbit and other species, but there are species differences in their distribution.
IT 21102-95-4, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rabbit .alpha.1b-adrenoceptor sequence and expression and pharmacol.

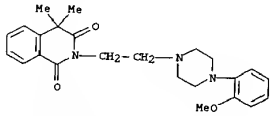
L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
comparison with other .alpha.1-adrenoceptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



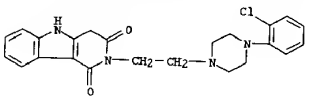
●2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:343282 CAPLUS
DOCUMENT NUMBER: 133:159627
TITLE: The ad hoc supermolecule approach to receptor ligand design
AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena e Reggio Emilia, Modena, 41100, Italy
SOURCE: THEOCHEM (2000), 503(1-2), 1-16
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Among the ligand design methods based on the theor. QSAR paradigm, the simple ad hoc supermol. approach is presented and applied to a highly non-congeneric set of .alpha.1-adrenergic receptor antagonists. The performance of the approach is satisfactory and highlights its (semi)quant. ligand design potentiality.
IT 67339-62-2 288073-22-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ad hoc supermol. approach to receptor ligand design)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



RN 288073-22-3 CAPLUS
CN 1H-Pyrido[4,3-b]indole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,5-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS

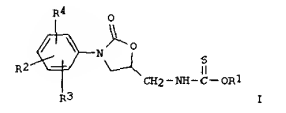
L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:335397 CAPLUS
DOCUMENT NUMBER: 132:334453
TITLE: Preparation of oxazolidinylmethylthiocarbamic acid derivatives as antibacterial agents
INVENTOR(S): Kado, Noriyuki; Tokuyama, Ryukou; Tsubouchi, Masatoshi; Tomita, Yayoi
PATENT ASSIGNEE(S): Hokuriku Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000027830	A1	20000518	WO 1999-JP6260	19991110
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000204084	A2	20000725	JP 1999-273230	19990927
EP 1130016	A1	20010905	EP 1999-971804	19991110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1998-320137 A 19981111
JP 1999-273230 A 19990927
WO 1999-JP6260 W 19991110
OTHER SOURCE(S): MARPAT 132:334453
GI

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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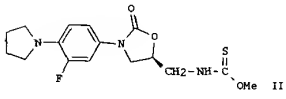


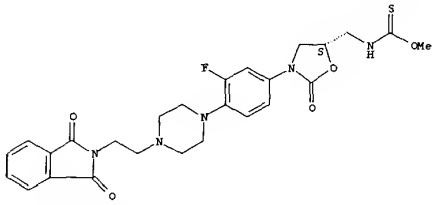
II

AB The title compds. I [R1 is optionally substituted alkyl or optionally substituted cycloalkyl; and R2, R3 and R4 are each independently hydrogen, halogeno, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted amino, optionally substituted alkanoyl, optionally substituted cycloalkyloxy contg. a heteroatom as the ring-constituting atom, or an optionally substituted satd. heterocyclic group, or alternatively any two of R2, R3 and R4 together with the benzene ring may form an optionally substituted fused hydrocarbon ring] are prepd. The title compd. II in vitro showed IC50 of 0.39 .mu.g/mL against S. aureus, vs. IC50 of 3.13 .mu.g/mL for linezolid.

IT **268208-40-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)
RN 268208-40-8 CAPLUS
CN Carbamothioic acid, {[(5S)-3-[4-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-1-piperazinyl]-3-fluorophenyl]-2-oxo-5-oxazolidinyl]methyl]-, O-methyl ester (9CI) (CA INDEX NAME)

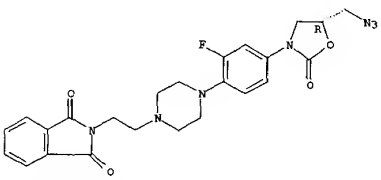
Absolute stereochemistry. Rotation (-).

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT **268208-92-0P 268209-56-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)
RN 268208-92-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[4-[(5R)-5-(azidomethyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

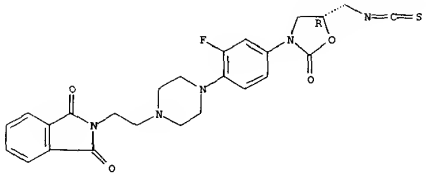
Absolute stereochemistry. Rotation (-).



RN 268209-56-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[2-fluoro-4-[(5R)-5-(isothiocyanatomethyl)-2-oxo-3-oxazolidinyl]phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:311250 CAPLUS
DOCUMENT NUMBER: 133:104983
TITLE: Synthesis and serotonin 2 (5-HT2) receptor antagonist activity of 5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related compounds
AUTHOR(S): Mizuno, Akira; Ogata, Atsuto; Kamei, Tomoe; Shibata, Makoto; Shimamoto, Tetsuo; Hayashi, Yasuhiro; Nakanishi, Kyoko; Takiguchi, Chikako; Oka, Naomi; Inomata, Norio
CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka, 618-8503, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(5), 623-635
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:104983
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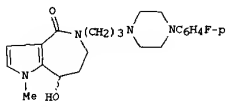


I

AB A series of 5-aminoalkylpyrrolo[3,2-c]azepine derivs. was synthesized and their serotonin 2 (5-HT2) receptor antagonist and antiplatelet aggregation activities were evaluated. 5-HT2 receptor antagonist activity was largely detd. by the nature of the substituent at the 8-position as well as the aminoalkyl group at the 5-position of the pyrrolo[3,2-c]azepine ring. Compd. I was recognized as having potent 5-HT2 receptor antagonist activity with weak .alpha.1 adrenoceptor blocking activity and no significant D2 receptor binding affinity. (.+-.)-I was resolved directly via diastereomeric salt formation and each enantiomer was evaluated. The 5-HT2 receptor antagonist activity of I was found to reside primarily in (-)-I (.alpha.-OH) (which was about 14-fold more potent than (+)-I (.beta.-OH) in isolated guinea pig arteries). Consequently, (S)-(-)-I (SUN C5174) displayed the overall best profile with potent 5-HT2 receptor antagonist activity (pA2=8.98.+-.0.06) and high selectivity vs. other

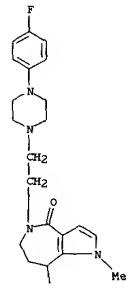
L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

receptors. SUN C5174 showed a marked inhibitory effect on the platelet aggregation induced by serotonin in combination with collagen and ADP in canine or human platelet-rich plasma (IC50=6.5 to 16 nM). SUN C5174 significantly inhibited the mortality rate in mouse acute pulmonary thromboembolitic death induced by collagen and serotonin at oral doses of 0.3 mg/kg or higher. SUN C5174 is currently undergoing clin. evaluation.

IT **191592-08-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and serotonin 2 (5-HT2) receptor antagonist activity of 5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related compds.)

RN 191592-08-2 CAPLUS
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A



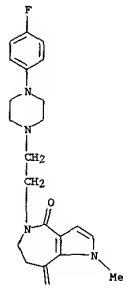
L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A

IT **191591-85-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and serotonin 2 (5-HT2) receptor antagonist activity of 5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related compds.)

RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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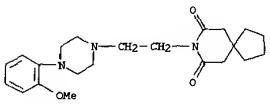
L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:309881 CAPLUS
DOCUMENT NUMBER: 133:69131
TITLE: Splice isoforms of .alpha.1a-adrenoceptor in rabbit
AUTHOR(S): Suzuki, Fumiko; Taniguchi, Takanobu; Takauji, Rumiko; Murata, Satoshi; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: British Journal of Pharmacology (2000), 129(8), 1569-1576
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two splice isoforms of rabbit .alpha.1a-adrenergic receptor (AR), (named .alpha.1a-OCU.2-AR and .alpha.1a-OCU.3-AR) have been isolated from the liver cDNA library in addn. to the previously reported isoform (.alpha.1a-OCU.1-AR). Although they have the identical splice position with human .alpha.1a-AR isoforms, the C-terminal sequences are distinct from those of human isoforms. Among these rabbit .alpha.1a-AR isoforms, there are no significant differences in pharmacol. properties: high affinity for prazosin, WB 4101, YMD-3213 and YM 617 and low affinity for BMY 7378, using COS-7 cells expressing each isoform by radioligand binding assay. Competitive reverse transcription-polymerase chain reaction (RT-PCR) anal. revealed that mRNA of .alpha.1a-ARs was expressed in liver, thoracic aorta, brain stem and thalamus of rabbit. The splice isoforms exhibited a distinct distribution pattern in rabbit; .alpha.1a-OCU.1-AR was expressed most abundantly in those tissues. CHO clones, stably expressing each isoforms with receptor d. 740 fmol mg-1 protein in .alpha.1a-OCU.1-AR, 1200 fmol mg-1 in .alpha.1a-OCU.2-AR and 570 fmol mg-1 in .alpha.1a-OCU.3-AR, resp., showed a noradrenaline-induced increase in inositol trisphosphate which was suppressed by prazosin. Noradrenaline elicited a concn.-dependent increase in extracellular acidification rate (EAR) in the CHO clones with pEC50 values of 6.19 for .alpha.1a-OCU.1-AR, 6.49 for .alpha.1a-OCU.2-AR and 6.58 for .alpha.1a-OCU.3-AR, resp. Noradrenaline caused a concn.-dependent increase in intracellular Ca2+ concn. ([Ca2+]i) in the CHO clones with pEC50 values of 6.14 for .alpha.1a-OCU.1-AR, 7.25 for .alpha.1a-OCU.2-AR and 7.70 for .alpha.1a-OCU.3-AR, resp. In conclusion, the present study shows the occurrence of three splice isoforms of rabbit .alpha.1a-AR, which are

L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
unique in C-terminal sequence and in tissue distribution. They show similar pharmacol. profiles in binding studies but .alpha.1a-OCU.3-AR had the highest potency of noradrenaline in functional studies in spite of the lowest receptor d. These findings suggest that the structure of C-terminus of .alpha.1a-ARs may give the characteristic functional profile.
IT **21102-95-4**, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.1a-adrenoceptor splice isoform sequence and functional expression and pharmacol. characterization in rabbit)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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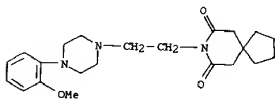
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 41 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:273553 CAPLUS
DOCUMENT NUMBER: 133:13034
TITLE: .alpha.1-Adrenoceptor subtypes mediating contractions of the rat mesenteric artery
AUTHOR(S): Hussain, M. B.; Marshall, I.
CORPORATE SOURCE: Department of Pharmacology, University College London, London, UK
SOURCE: European Journal of Pharmacology (2000), 395(1), 69-76
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.1-adrenoceptor subtype(s) mediating contractions of the rat mesenteric artery were investigated using the agonists methoxamine, cirazoline, P 7480 and subtype-selective antagonists including BMY 7378. The pA2 or apparent pKB values of antagonists against methoxamine contractions correlated best with its pKi values at the cloned .alpha.1b-(0.98), with cirazoline, antagonists affinities correlated equally well with those at .alpha.1a-(0.79) or the .alpha.1b-(0.81) while with P 7480 antagonist affinities correlated best with the .alpha.1d-adrenoceptor subtype (0.94). The low affinity est. for 5-methylurapidil (7.5) against the .alpha.1a-selective cirazoline suggests an .alpha.1A-subtype mediating contraction is unlikely. Shallow Schild plot slopes of subtype selective antagonists against all three agonists are consistent with heterogeneity of .alpha.1-adrenoceptors. P 7480 (putative .alpha.1D-adrenoceptor-selective) acts primarily at this subtype and at another which is more likely to be an .alpha.1B- than an .alpha.1A-adrenoceptor. The results with both agonists and antagonists are consistent with contractions of the rat mesenteric artery being mediated via the .alpha.1D- and possibly .alpha.1B-adrenoceptor.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor subtypes mediating contractions of rat mesenteric artery and pharmacol. characterization thereof)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 41 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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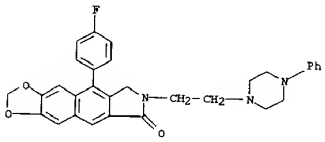
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 42 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
inhibitors)
RN 263018-67-3 CAPLUS
CN 6H-1,3-Benzodioxolo[5,6-f]isoindol-6-one, 9-(4-fluorophenyl)-7,8-dihydro-7-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 42 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:218572 CAPLUS
DOCUMENT NUMBER: 132:260701
TITLE: Tricyclic compounds, their preparation, and cyclic GMP phosphodiesterase inhibitors
INVENTOR(S): Tsuburai, Shogo; Ooi, Takayuki; Tarui, Naoki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 71 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000095759	A2	20000404	JP 1999-204103	19990719
PRIORITY APPLN. INFO.:			JP 1998-204963	19980721
OTHER SOURCE(S):		MARPAT 132:260701		

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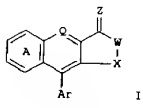


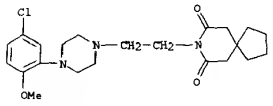
AB Title inhibitors contain tricyclic compds. I [ring A = (substituted) benzene ring; W = (substituted) NH; Q = CR, N; R = H, (substituted) alkyl, (substituted) alkoxy; X = (substituted) C1-2 alkylene; Z = H2, O; Ar = (substituted) arom. hydrocarbyl, (substituted) arom. heterocyclyl] or their salts. (6-Bromo-1,3-benzodioxol-5-yl)methanol (4.0 g) was treated with BuLi followed by 2.3 g 4-FC6H4CN in THF/hexane at room temp. for 2 h and treated with 3.5 g maleimide and p-MeC6H4SO3H in PhMe under reflux for 15 h to give 5.6 g I (ring A = 1,3-benzodioxole, W = NH, Q = CH, X = CO, Z = O, Ar = C6H4F-p). I (ring A = 1,3-benzodioxole, W = 4-pyridylmethylimino, Q = CH, X = CH2, Z = O, Ar = C6H4F-p) in vitro inhibited recombinant human phosphodiesterase with IC50 of 8.3 nM. Formulation examples are given.

IT **263018-67-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tricyclic compds. as cyclic GMP phosphodiesterase

L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:171777 CAPLUS
DOCUMENT NUMBER: 132:303466
TITLE: Effects of intracavernous administration of selective antagonists of .alpha.1-adrenoceptor subtypes on erection in anesthetized rats and dogs
AUTHOR(S): Sironi, Giorgio; Colombo, Davide; Poggesi, Elena; Leonardi, Amedeo; Testa, Rodolfo; Rampin, Olivier; Bernabe, Jacques; Giuliano, Francois
CORPORATE SOURCE: Pharmaceutical R and D Division, Milan, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 292(3), 974-981
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

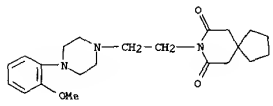
AB The proerectile properties of three novel .alpha.1-adrenoceptor (.alpha.1-AOR) antagonists with different profiles of selectivity for the .alpha.1-ADR subtypes have been evaluated in anesthetized rats and dogs on intracavernous (IC) injection, in comparison with prazosin and phentolamine. In rats, the tested compds. decreased blood pressure (BP) and increased IC pressure (ICP), as well as the ratio ICP/BP. Rec 15/2841 (.alpha.1a- plus .alpha.1L-AOR-selective antagonist) and Rec 15/2615 (.alpha.1b-AOR selective) were the most potent compds. The ICP/BP ratios calcd. after injection of Rec 15/3039 (.alpha.1d-ADR selective) were not markedly different from those obsd. after vehicle injection. Prazosin and phentolamine proved poorly active, their main effect being hypotension. Approx. ED25 values (dose of compd. in micrograms inducing 25% increase of ICP/BP ratio) were Rec 15/2615 (22 .mu.g/kg) >= Rec 15/2841 (29 .mu.g/kg) > prazosin (136 .mu.g/kg) > phentolamine (1298 .mu.g/kg) > Rec 15/3039 (9600 .mu.g/kg). Submaximal stimulation of the cavernous nerve elicited an ICP rise whose amplitude was not altered by Rec compds. In contrast, prazosin and phentolamine decreased this ICP rise. All compds. but 15/3039 induced significant increase of the ICP/BP ratio in dogs. Rec 15/2615 proved to be the most interesting compd., inducing significant increases of ICP/BP at doses practically devoid of effects on BP. The rank order of potency in dog in increasing the ICP/BP ratio was similar to that obsd. in rats. Only at the highest doses tested, all compds., except Rec 15/3039, decreased the ICP rise elicited by submaximal stimulation of

L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
the cavernous nerve. Our data demonstrate that the .alpha.1b- and .alpha.1L-ADR subtypes are functionally relevant for the erectile function
in these models, and that .alpha.1b- and/or .alpha.1L-ADR subtypes selective antagonists could represent a real advantage in erectile dysfunction therapy.
IT **252240-56-5**, REC 15/3039
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(effects of intracavernous administration of selective antagonists of
.alpha.1-adrenoceptor subtypes on erection in anesthetized rats and
dogs)
RN 252240-56-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:125868 CAPLUS
DOCUMENT NUMBER: 132:245855
TITLE: Ligand design for .alpha.1-adrenoceptor subtype selective antagonists
AUTHOR(S): Bremner, John B.; Coban, Burak; Griffith, Renate; Groenewoud, Karina M.; Yates, Brian F.
CORPORATE SOURCE: Department of Chemistry, University of Wollongong, Wollongong, 2522, Australia
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(1), 201-214
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .alpha.1-Adrenoceptors have three subtypes and drugs interacting selectively with these subtypes could be useful in the treatment of a variety of diseases. In order to gain an insight into the structural principles governing subtype selectivity, ligand based drug design (pharmacophore development) methods have been used to design a novel 1,2,3-thiadiazole ring D analog of the aporphine system. Synthesis and
testing of this compd. as a ligand on cloned and expressed human .alpha.1-adrenoceptors is described. Low binding affinity was found, possibly due to an unfavorable electrostatic potential distribution. Pharmacophore models for antagonists at the three adrenoceptor sites (.alpha.1A, .alpha.1B, .alpha.1D) were generated from a no. of different
training sets and their value for the design of new selective antagonists
discussed. The first preliminary antagonist pharmacophore model for the
.alpha.1D adrenoceptor subtype is also reported.
IT **21102-95-4**, BMY-7378 **255893-38-0**, SNAP 8719
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(ligand design for .alpha.1-adrenoceptor subtype selective antagonists)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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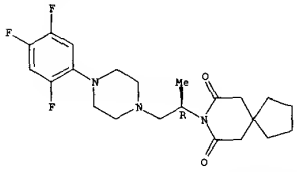
L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 255893-38-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:84765 CAPLUS
DOCUMENT NUMBER: 132:122634
TITLE: Preparation of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers
INVENTOR(S): Anand, Nitya; Sinha, Neelima; Jain, Sanjay; Mehta, Anita; Saxena, Anil Kumar; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005206	A1	20000203	WO 1999-IB140	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6083950	A	20000704	US 1998-120265	19980721
AU 9919797	A1	20000214	AU 1999-19797	19990126
WO 2000005205	A1	20000203	WO 1999-IB1296	19990716
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BR 9912318	A	20010502	BR 1999-12318	19990716
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L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

US 1998-120265	A	19980721
IN 1997-DE3260	A	19971113
IN 1997-DE3261	A	19971113
WO 1999-IB140	W	19990126
WO 1999-IB1296	W	19990716

OTHER SOURCE(S): MARPAT 132:122634

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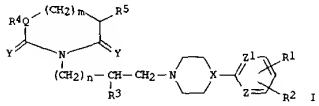

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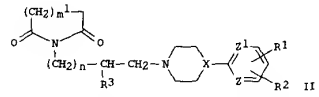


II

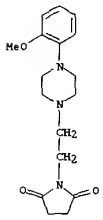
AB The title compds. [I; Y = O, S; Q, X, Z, and Z1 = CH, N; m = 0-3, n = 0-4; R1, R2 = H, F, Cl, etc.; R3 = H, R6, OH, OR6; R6 = alkyl; R4, R5 = H, alkyl, (un)substituted Ph, etc.] and more preferred compds. II [m1 = 1-4] which have been found to exhibit selective .alpha.1A adrenergic activity, were prepd. Thus, reacting 2,5-dioxopyrrolidine with 1-[4-(4-fluorophenyl)piperazin-1-yl]-3-chloropropane in the presence of K2CO3 and Bu4NBr in Me2CO afforded 65% II [m1 = 1; n = 1; X = N; Z = Z1 = CH; R1 = 4-F; R2 = R3 = H]. Biol. data for compds. II were given. The compds. I and II are useful for treatment of disease conditions, such as peripheral vascular disease, congestive heart failure, hypertension and esp. benign prostatic hypertrophy.

IT **255861-61-1P 255861-79-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers)

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 255861-61-1 CAPLUS

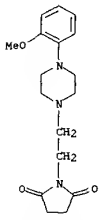
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 255861-79-1 CAPLUS

CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

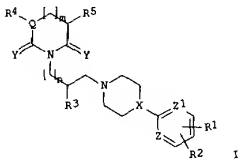
L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS

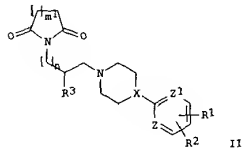
ACCESSION NUMBER: 2000:84764 CAPLUS
DOCUMENT NUMBER: 132:107963
TITLE: Preparation of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers
INVENTOR(S): Anand, Nitya; Sinha, Neelima; Jain, Sanjay; Mehta, Anita; Saxena, Anil Kumar; Gupta, Jang Bahadur
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005205	A1	20000203	WO 1999-IB1296	19990716
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6083950	A	20000704	US 1998-120265	19980721
WO 2000005206	A1	20000203	WO 1999-IB14D	19990126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MX, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9946410	A1	20000214	AU 1999-46410	19990716
BR 9912318	A	20010502	BR 1999-12318	19990716
EP 1097134	A1	20010509	EP 1999-929633	19990716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IE, SI, LT, LV, FI, RO
JP 2002521362 T2 20020716 JP 2000-561162 19990716
PRIORITY APPLN. INFO.: US 1998-120265 A 19980721
WO 1999-IB140 W 19990126
IN 1997-DE3260 A 19971113
IN 1997-DE3261 A 19971113
IB 1999-IB990014 0A 19990126
WO 1999-IB1296 W 19990716
OTHER SOURCE(S): MARPAT 132:107963
GI



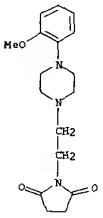
I



II

AB The title compds. [I: Y = O, S; Q, X, Z, and Z1 = CH, N; m = 0-3, n = 0-4; R1, R2 = H, F, Cl, etc.; R3 = H, R6, OH, OR6; R6 = alkyl; R4, R5 = H, alkyl, (un)substituted Ph, etc.] and more preferred compds. II [m1 = 1-4] which have been found to exhibit selective .alpha.1A adrenergic activity, were prepd. Thus, reacting 2,5-dioxopyrrolidine with 1-[4-(4-fluorophenyl)piperazin-1-yl]-3-chloropropane in the presence of K2CO3 and Bu4NBr in Me2CO afforded 65% II [m1 = 1; n = 1; X = N; Z = Z1 = CH; R1 = 4-F; R2 = R3 = H]. Biol. data for compds. II were given. The compds. I

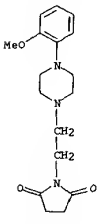
L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and II are useful for treatment of disease conditions, such as peripheral vascular disease, congestive heart failure, hypertension and esp. benign prostatic hypertrophy.
IT **255861-61-1P 255861-79-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers)
RN 255861-61-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

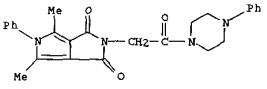
RN 255861-79-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



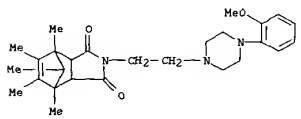
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 47 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:74842 CAPLUS
DOCUMENT NUMBER: 132:222466
TITLE: Synthesis of some N-substituted 3,4-pyrroledicarboximides as potential CNS depressive agents
AUTHOR(S): Malinka, W.; Sieklucka-Dziuba, M.; Rajtar, G.; Rejdak, R.; Rejdak, K.; Kleinrok, Z.
CORPORATE SOURCE: Department of Chemistry of Drugs, Wroclaw Medical University, Lublin, Pol.
SOURCE: Pharmazie (2000), 55(1), 9-16
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several novel N-substituted 3,4-pyrroledicarboximides were prepd. and eleven representatives were examd. in a series of in vivo CNS tests. A few of these compds. displayed a similar profile of biol. selectivity to that of 3,4-pyrroledicarboximides described previously; their structure-activity relationships are discussed.
IT **261164-81-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of pyrroledicarboximides as potential CNS depressive agents)
RN 261164-81-2 CAPLUS
CN Piperazine, 1-[(3,5-dihydro-4,6-dimethyl-1,3-dioxo-5-phenylpyrrolo[3,4-c]pyrrol-2(1H)-yl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

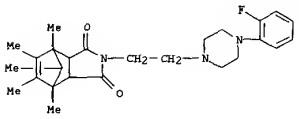
L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:74841 CAPLUS
DOCUMENT NUMBER: 132:222411
TITLE: Synthesis of new derivatives of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with an expected anxiolytic activity
AUTHOR(S): Kossakowski, J.; Kusmierczyk, J.
CORPORATE SOURCE: Department of Medical Chemistry, Medical University of Warsaw, Pol.
SOURCE: Pharmazie (2000), 55(1), 5-8
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The prepn. of a no. of derivs. of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with potential anxiolytic activity has been described. The aim of our study was to obtain new analogs of tandospirone, that is derivs. of cyclic imides.
IT **261160-88-7P 261160-90-1P 261160-92-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and anxiolytic activity of pentamethylbicycloheptenedicarboximides)
RN 261160-88-7 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 3a,4,7,7a-tetrahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,5,6,7,8-pentamethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

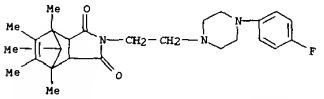
RN 261160-90-1 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 261160-92-3 CAPLUS
CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl- (9CI) (CA INDEX NAME)



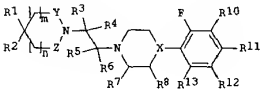
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:68449 CAPLUS
DOCUMENT NUMBER: 132:107961
TITLE: Preparation of 8-[2-piperazino(or piperidino)ethyl]-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor
INVENTOR(S): Konkel, Michael; Wetzel, John M.; Noble, Stewart; Gluchowski, Charles; Craig, Douglas A.
PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004012	A1	20000127	WO 1999-US16101	19990716
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9952146	A1	20000207	AU 1999-52146	19990716
EP 1100794	A1	20010523	EP 1999-937273	19990716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520408	T2	20020709	JP 2000-560118	19990716
US 2002028760	A1	20020307	US 2001-764710	20010117

PRIORITY APPLN. INFO.: US 1998-118323 A2 19980717
WO 1999-US16101 W 19990716
OTHER SOURCE(S): MARPAT 132:107961
GI

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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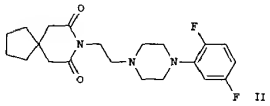
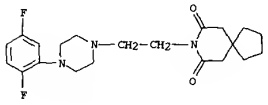


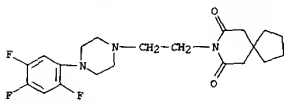
II

AB The title compds. [I; n = 0-2; m = 0-2; Y = CH2, CO, CS; Z = CH2, CO, CS; R1, R2 = H, alkyl, alkoxy, etc.; R3 = H, alkyl, alkenyl, etc.; R4 = H, Me; R5 = H, alkyl, alkenyl, etc.; R6 = H, alkyl, alkenyl, etc.; R7 = H, alkyl, alkenyl, etc.; R8 = H, Me; R10 = H, F; R11 = H, F, Cl, etc.; R12 = H, F, Cl, etc.; R13 = H, F; X = N, CH] which binds selectively to a human .alpha.1d adrenergic receptor, and are useful in treating hypertension, Raynaud's disease, and urinary incontinence, were prepd. and formulated.
Thus, heating 1-(2,5-difluorophenyl)piperazine with 8-(2-chloroethyl)-8-azaspiro[4.5]decane (prepns. were given) afforded II which showed pKi of 9.0 at .alpha.1d receptor.
IT **255893-35-7P 255893-36-8P 255893-37-9P**
255893-38-0P 255893-39-1P 255893-40-4P
255893-42-6P 255893-43-7P 255893-44-8P
255893-45-9P 255893-46-0P 255893-48-2P
255893-50-6P 255893-51-7P 255893-52-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 8-(2-piperazino(or piperidino)ethyl)-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor)
RN 255893-35-7 CAPLUS

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

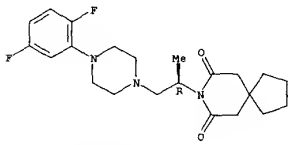


RN 255893-36-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-37-9 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

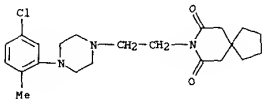
Absolute stereochemistry.



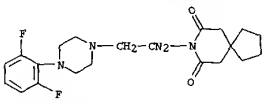
RN 255893-38-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

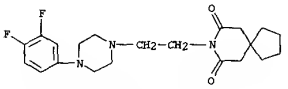
L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 255893-42-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-43-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,6-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



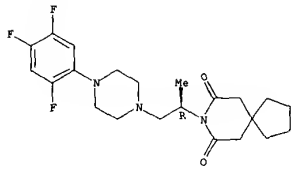
RN 255893-44-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3,4-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-45-9 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-phenyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

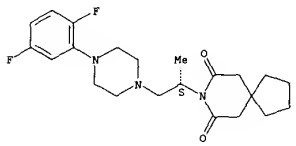
Absolute stereochemistry.

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



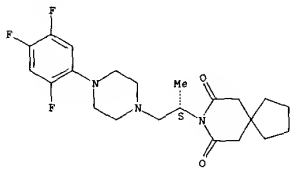
RN 255893-39-1 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

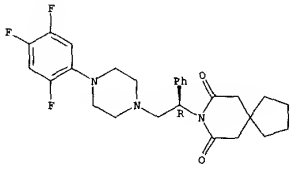


RN 255893-40-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

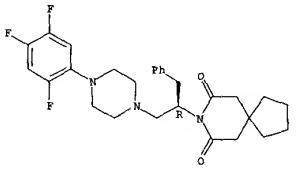


L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

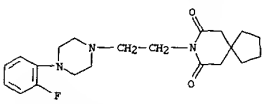


RN 255893-46-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-(phenylmethyl)-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

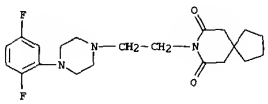


RN 255893-48-2 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



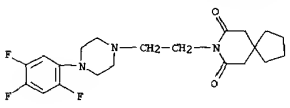
RN 255893-50-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-difluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 255893-51-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

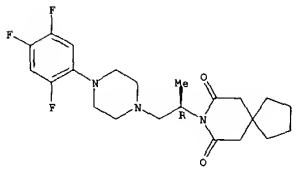


● 6/5 HCl

RN 255893-52-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

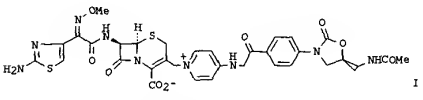


● HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:26717 CAPLUS
DOCUMENT NUMBER: 132:207679
TITLE: Synthesis and in vitro antibacterial activity of quaternary ammonium cephalosporin derivatives bearing oxazolidinone moiety
AUTHOR(S): Chung, In Hwa; Kim, Choong Sup; Seo, Jae Hong; Chung, Bong Young
CORPORATE SOURCE: Biochemicals Research Center, Korea Institute of Science and Technology, Seoul, 130-650, S. Korea
SOURCE: Archives of Pharmacal Research (1999), 22(6), 579-584
CODEN: APHRDQ; ISSN: 0253-6269
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

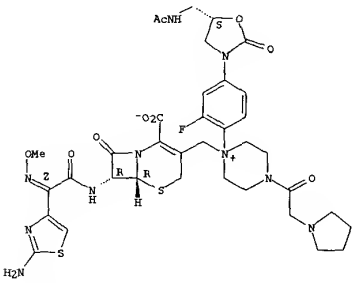
AB Several oxazolidinones having amine moiety were prepd. to form a quaternary ammonium salt with cephalosporin nucleus, and antibacterial activity of the quaternary ammonium cephalosporin derivs. (e.g., I) bearing oxazolidinone moiety were examd. particularly with expectation of dual activity. However, the cephalosporin-oxazolidinone compds. revealed rather weaker antibacterial activity in vitro than their parent oxazolidinone and cephalosporin without showing any characteristic activity as expected.

IT **260262-92-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antibacterial activity of quaternary ammonium oxazolidinonocephalosporin derivs.)

RN 260262-92-8 CAPLUS
CN Piperazinium, 1-[4-[(5S)-5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-[[(6R,7R)-7-[[(2Z)-(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-4-(1-pyrrolidinylacetyl)-, inner salt (9CI) (CA INDEX NAME)

L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

Absolute stereochemistry.
Double bond geometry as shown.

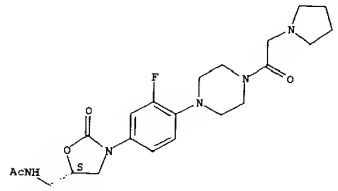


IT **260262-82-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and antibacterial activity of quaternary ammonium oxazolidinonocephalosporin derivs.)

RN 260262-82-6 CAPLUS
CN Acetamide, N-[[(5S)-3-[3-fluoro-4-[4-(1-pyrrolidinylacetyl)-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

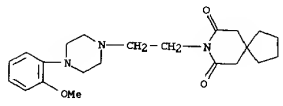
L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

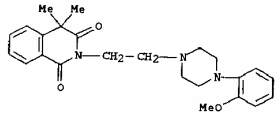
L14 ANSWER 51 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:9434 CAPLUS
DOCUMENT NUMBER: 132:146156
TITLE: Relevance of theoretical molecular descriptors in quantitative structure-activity relationship analysis of .alpha.1-adrenergic receptor antagonists
AUTHOR(S): Menziani, M. C.; Montorsi, M.; De Benedetti, P. G.; Karelson, M.
CORPORATE SOURCE: Department of Chemistry, University of Modena and Reggio Emilia, Modena, 41100, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(11), 2437-2451
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A quant. structure-activity relationship (QSAR) study of a wide series of structurally diverse .alpha.1-adrenergic receptor antagonists was performed using the CODESSA (Comprehensive Descriptors for Structural and Statistical Anal.) technique. Theor. descriptors derived on a single structure and ad hoc defined size and shape descriptors were considered in the attempt of describing information relevant to receptor interaction. The relative effectiveness of these two classes of parameters in developing QSAR models for native (.alpha.1A and .alpha.1B) and cloned (.alpha.1a, .alpha.1b, and .alpha.1d) adrenergic receptor binding affinity, functional activity of vascular and lower urinary tract tissues, and in vitro and in vivo selectivity was evaluated.
IT **21102-95-4**, BMY 7378 **67339-62-2**, ARC 239 **99718-67-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(relevance of theor. mol. descriptors in QSAR anal. of .alpha.1-adrenergic receptor antagonists)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 51 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

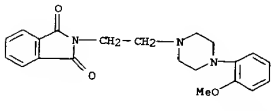


●2 HCl

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



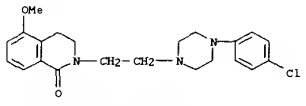
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



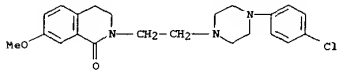
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 52 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:815373 CAPLUS
DOCUMENT NUMBER: 132:165762
TITLE: A Structure-Affinity Relationship Study on Derivatives of N-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a High-Affinity and Selective D4 Receptor Ligand
AUTHOR(S): Perrone, Roberto; Berardi, Francesco; Colabufo, Nicola A.; Leopoldo, Marcello; Tortorella, Vincenzo
CORPORATE SOURCE: Dipartimento Farmaco-Chimico, Universita di Bari, Bari, 70126, Italy
SOURCE: Journal of Medicinal Chemistry (2000), 43(2), 270-277
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a high-affinity and selective dopamine D4 receptor ligand, was chosen as a lead, and structural modifications were done on its amide bond and on its alkyl chain linking the benzamide moiety to the piperazine ring and by prepg. some semirigid analogs. The binding profile at dopamine D4 and dopamine D2, serotonin 5-HT1A, and adrenergic .alpha.1 receptors of 16 new compds. was detd. From the results emerged that the modification of the amide bond and the elongation of the intermediate alkyl chain caused a decrease in dopamine D4 receptor affinity. All prepd. semirigid analogs displayed D4 receptor affinity values in the same range of the opened counterparts.
IT **258882-65-4P 258882-66-5P 258882-78-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of derivs. of [[(chlorophenyl)piperazinyl]ethyl]methoxybenzamide as selective D4 receptor ligand)
RN 258882-65-4 CAPLUS
CN 1(2H)-Isoquinolinone, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-dihydro-5-methoxy- (9CI) (CA INDEX NAME)

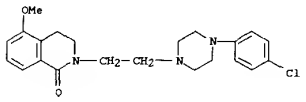
L14 ANSWER 52 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 258882-66-5 CAPLUS
CN 1(2H)-Isoquinolinone,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-
dihydro-7-methoxy- (9CI) (CA INDEX NAME)



RN 258882-78-9 CAPLUS
CN 1(2H)-Isoquinolinone,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-
dihydro-5-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)

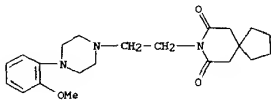


●2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:805403 CAPLUS
DOCUMENT NUMBER: 132:117709
TITLE: Constitutive Gi2-dependent activation of adenylyl cyclase type II by the 5-HT1A receptor. Inhibition by anxiolytic partial agonists
AUTHOR(S): Albert, Paul R.; Sajedi, Naghmeh; Lemonde, Sylvie; Ghahremani, Mohammad H.
CORPORATE SOURCE: Neuroscience Research Institute, Departments of Medicine and Cellular and Molecular Medicine, University of Ottawa, Ottawa, ON, K1H 8M5, Can.
SOURCE: Journal of Biological Chemistry (1999), 274(50), 35469-35474
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-HT1A receptor is implicated in depression and anxiety. This receptor couples to Gi proteins to inhibit adenylyl cyclase (AC) activity but can stimulate AC in tissues (e.g., hippocampus) that express ACII. The role of ACII in receptor-mediated stimulation of cAMP formation was exam. in HEK-293 cells transfected with the 5-HT1A receptor, which mediated inhibition of basal and Gs-induced cAMP formation in the absence of ACII. In cells cotransfected with 5-HT1A receptor and ACII plasmids, 5-HT1A agonists induced a 1.5-fold increase in cAMP level. Cotransfection of 5-HT1A receptor, ACII, and G.alpha.i2, but not G.alpha.i1, G.alpha.i3, or G.alpha.o, resulted in an agonist-independent 6-fold increase in the basal cAMP level, suggesting that Gi2 preferentially coupled the receptor to ACII. The 5-HT1B receptor also constitutively activated ACII. Constitutive activity of the 5-HT1A receptor was blocked by pertussis toxin and the G.beta..gamma. antagonist, .beta.CT, suggesting an important role for G.beta..gamma.-mediated activation of ACII. The Thr 149 .fwdarw. Ala mutation in the second intracellular domain of the 5-HT1A receptor disrupted G.beta..gamma.-selective activation of ACII. Spontaneous 5-HT1A receptor activity was partially attenuated by 5-HT1A receptor partial agonists with anxiolytic activity (e.g., buspirone and flesinoxan) but was not altered by full agonists or antagonists. Thus, anxiolytic activity may involve inhibition of spontaneous 5-HT1A receptor activity.
IT **21102-95-4**, BMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

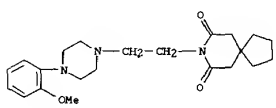
L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(constitutive Gi2-dependent activation of adenylyl cyclase type II by 5-HT1A receptor and inhibition by anxiolytic partial agonists)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:750562 CAPLUS
DOCUMENT NUMBER: 132:216950
TITLE: Interaction of clozapine and other antipsychotic drugs with human .alpha.1-adrenergic receptor subtypes
AUTHOR(S): Brooks, Karen M.; Cai, Jidong; Sandrasagra, Anthony; Roehr, Joachim E.; Errazo, Rowena; Vargas, Hugo M.
CORPORATE SOURCE: General Pharmacology, Hoechst Marion Roussel, Inc., Bridgewater, NJ, 08807-0800, USA
SOURCE: Proceedings of the Western Pharmacology Society (1999), 42, 67-69
CODEN: PWPSA8; ISSN: 0083-8969
PUBLISHER: Western Pharmacology Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antipsychotic drugs bind to a variety of neurotransmitter receptors. Blockage of brain .alpha.1-adrenergic receptors may contribute to the clin. efficacy and low extrapyramidal side effects of atypical antipsychotics. The authors evaluated clozapine and other antipsychotic drugs for interaction with human .alpha.1-adrenergic receptor subtypes. The atypical antipsychotic drug clozapine demonstrated high affinity for each of the recombinant human .alpha.1-adrenergic receptors.
IT **21102-95-4**, BMY 7378
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interaction of clozapine and other antipsychotic drugs with human .alpha.1-adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4,5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

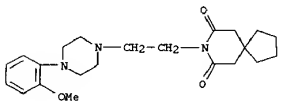


●2 HCl

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:750546 CAPLUS
DOCUMENT NUMBER: 132:216777
TITLE: Segmental differences in rat aorta contraction induced
by phenylephrine in aortic rings
AUTHOR(S): Asbun-Bojalil, Juan; Escalante-Acosta, Bruno; Ceballos-Reyes, Guillermo; Ocharan-Hernandez, Maria
Esther; Castillo-Henkel, Enrique F.; Castillo-Henkel, Carlos
CORPORATE SOURCE: Seccion de Estudios de Posgrado e Investigacion, Escuela Superior de Medicina del Instituto Politecnico
Nacional, Mexico, Mex.
SOURCE: Proceedings of the Western Pharmacology Society (1999), 42, 23-24
CODEN: PWPSA8; ISSN: 0083-8969
PUBLISHER: Western Pharmacology Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was noted that vascular reactivity may differ between regions of the same vessel. The aim of the study was to evaluate the possibility of segmental differences in rat aorta contraction induced by phenylephrine. Concn.-response curves to phenylephrine obtained in thoracic and abdominal aortic rings with or without endothelium did not differ quant.
IT **21102-95-4**, BMY 7378
RL: BSU (Biological study, unclassified); BIOL (Biological study) (segmental differences in rat aorta contraction induced by phenylephrine)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

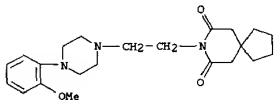
L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:723048 CAPLUS
DOCUMENT NUMBER: 131:346557
TITLE: Method using .alpha.1D-adrenergic antagonists for treating bladder and lower urinary tract syndromes, and screening method
INVENTOR(S): Schwinn, Debra A.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957131	A1	19991111	WO 1999-US9846	19990506
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2327543	AA	19991111	CA 1999-2327543	19990506
AU 9938830	A1	19991123	AU 1999-38830	19990506
EP 1075486	A1	20010214	EP 1999-921690	19990506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002513799	T2	20020514	JP 2000-547100	19990506

PRIORITY APPLN. INFO.: US 1998-84479P P 19980506
WO 1999-US9846 W 19990506

AB The invention relates to bladder and lower urinary tract syndromes, particularly, irritative symptoms, and to a method of treating them using an .alpha.1D-adrenergic receptor (.alpha.1DAR) antagonists. Also provided is a method of screening compds. for their ability to serve as .alpha.1DAR selective antagonists.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

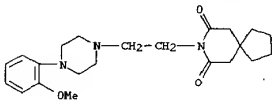
L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(Uses)
(.alpha.1D-adrenergic antagonists for treating bladder and lower urinary tract syndromes, and screening method)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

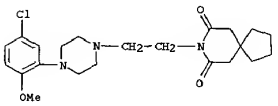
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 252240-56-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



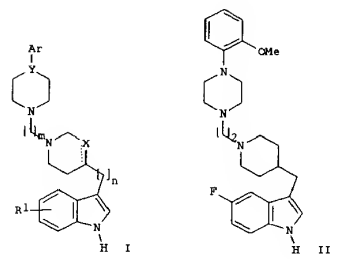
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:709584 CAPLUS
DOCUMENT NUMBER: 132:30765
TITLE: Inverse agonism and neutral antagonism at .alpha.1a-
and .alpha.1b-adrenergic receptor subtypes
AUTHOR(S): Rossier, Olivier; Abuin, Liliane; Fanelli, Francesca;
Leonardi, Amedeo; Cotecchia, Susanna
CORPORATE SOURCE: Institute of Pharmacology and Toxicology, Universite
de Lausanne, Lausanne, Switz.
SOURCE: Molecular Pharmacology (1999), 56(5), 858-866
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have characterized the pharmacol. antagonism, i.e., neutral antagonism
or inverse agonism, displayed by a no. of .alpha.-blockers at two .alpha.1-adrenergic receptor (AR) subtypes, .alpha.1a- and .alpha.1b-AR.
Constitutively activating mutations were introduced into the .alpha.1a-AR
at the position homologous to A293 of the .alpha.1b-AR where activating
mutations were previously described. Twenty-four .alpha.-blockers differing in their chem. structures were initially tested for their effect
on the agonist-independent inositol phosphate response mediated by the constitutively active A271E and A293E mutants expressed in COS-7 cells. A
selected no. of drugs also were tested for their effect on the small, but
measurable spontaneous activity of the wild-type .alpha.1a- and .alpha.1b-AR expressed in COS-7 cells. The results of our study demonstrate that a large no. of structurally different .alpha.-blockers
display profound neg. efficacy at both the .alpha.1a- and .alpha.1b-AR subtypes. For other drugs, the neg. efficacy varied at the different constitutively active mutants. The most striking difference concerns a
group of N-arylpiperazines, including 8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5] decane-7,9-dione (REC 15/3039), REC 15/2739, and REC 15/3011, which are inverse agonists with profound neg.
efficacy at the wild-type .alpha.1b-AR, but not at the .alpha.1a-AR.
IT **21102-95-4**, BMY 7378 **252240-56-5**, REC 15/3039
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(inverse agonism and neutral antagonism at .alpha.1a- and .alpha.1b-adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 58 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:708760 CAPLUS
DOCUMENT NUMBER: 131:310650
TITLE: Preparation of indolyl derivatives as serotonergic agents
INVENTOR(S): Kelly, Michael Gerard; Kang, Young Hee
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXO2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955695	A1	19991104	WO 1999-US9181	19990428
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330437	AA	19991104	CA 1999-2330437	19990428
AU 9939670	A1	19991116	AU 1999-39670	19990428
EP 1073651	A1	20010207	EP 1999-922739	19990428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002513016	T2	20020508	JP 2000-545855	19990428

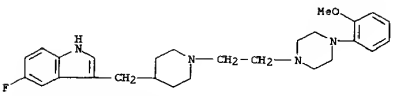
PRIORITY APPLN. INFO.: US 1998-69043 A 19980429
WO 1999-US9181 W 19990428
OTHER SOURCE(S): MARPAT 131:310650
GI



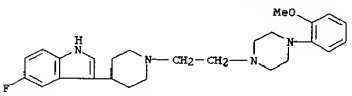
AB The title compds. [I; R1 = H, OH, OR2, halo (F, Cl, Br, I); R2 = lower alkyl; n = 0-2; X = CH, CH2; m = 2-4; Y = N, CH; Ar = (un)substituted aryl, heteroaryl] or their pharmaceutically acceptable salts, useful for the inhibition of serotonin uptake and the treatment of CNS disorders, particularly depression and anxiety. Thus, reaction of 4-(5-fluoro-1H-indol-3-ylmethyl)piperidine with 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine in the presence of K2CO3 and KI in MeCN afforded 80% II which showed Ki of 4.8 nM against [3H]-paroxetine binding.

IT **247911-01-9P 247911-02-0P 247911-05-3P 247911-06-4P 247911-07-5P 247911-08-6P 247911-09-7P 247911-12-2P 247911-14-4P 247911-15-5P 247911-16-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of indolyl derivs. as serotonergic agents)

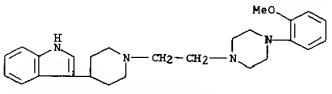
RN 247911-01-9 CAPLUS
CN 1H-Indole, 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



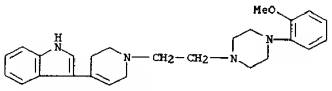
RN 247911-02-0 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



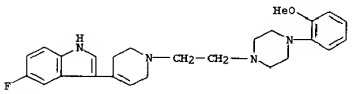
RN 247911-05-3 CAPLUS
CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



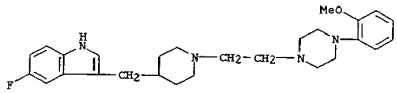
RN 247911-06-4 CAPLUS
CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



RN 247911-07-5 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)

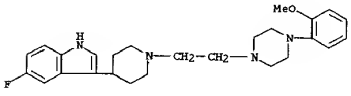


RN 247911-08-6 CAPLUS
CN 1H-Indole, 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 247911-09-7 CAPLUS
CN 1H-Indole, 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



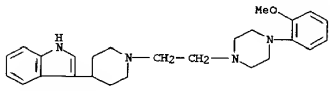
●2 HCl

RN 247911-12-2 CAPLUS
CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 247911-05-3

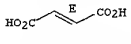
CMF C26 H34 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

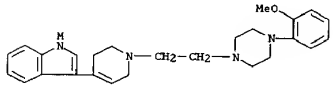
Double bond geometry as shown.



RN 247911-14-4 CAPLUS
CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

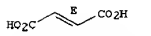
CRN 247911-06-4
CMF C26 H32 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

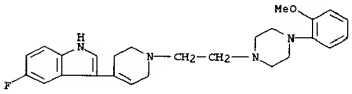
Double bond geometry as shown.



RN 247911-15-5 CAPLUS
CN 1H-Indole,
5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

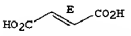
CRN 247911-07-5
CMF C26 H31 F N4 O



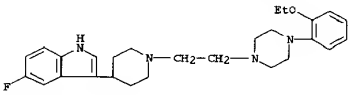
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 247911-16-6 CAPLUS
CN 1H-Indole,
3-[1-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-5-fluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

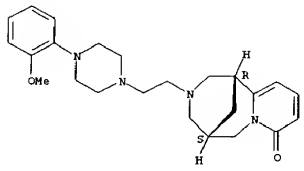
FORMAT

L14 ANSWER 59 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:571555 CAPLUS
DOCUMENT NUMBER: 131:337220
TITLE: Synthesis and preliminary pharmacological evaluation of some cytisine derivatives
AUTHOR(S): Boido, Caterina Canu; Sparatore, Fabio
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Genova, Genoa, 3-16132, Italy
SOURCE: Farmaco (1999), 54(7), 438-451
CODEN: FRMCES; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thirty-one N-derivs. of cytisine were prepd. to modify the pharmacol. profile and to obtain compds. of potential therapeutic interest either at a peripheral or central level, particularly as nicotinic ligands with improved ability to cross the blood-brain barrier. With the introduction of different kinds of substituents on the basic nitrogen of cytisine a variety of activities were obsd., both in vivo (analgesic, dopamine antagonism, antihypertensive, inhibition of stress-induced ulcers, antiinflammatory, protection from PAF-induced mortality, hypoglycemic) and in vitro (pos. cardio-inotropic, .beta.-adrenergic antagonism, .alpha.1- and .alpha.2-antagonism, inhibition of PAF-induced platelet aggregation). Six randomly selected compds. were tested for the ability to recognize a central nicotinic receptor and four of them exhibited Ki values in the range 30-163 nM.

IT **249907-28-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of cytisine derivs. and their preliminary pharmacol. evaluation)
RN 249907-28-6 CAPLUS
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride, (1R,5S)- (9CI) (CA INDEX NAME)

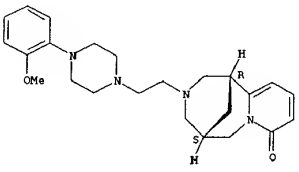
Absolute stereochemistry.



●2 HCl

IT **249906-94-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of cytisine derivs. and their preliminary pharmacol. evaluation)
RN 249906-94-3 CAPLUS
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:565907 CAPLUS
DOCUMENT NUMBER: 131:194295
TITLE: Agents, and combinations thereof, with serotonin-related activity for the treatment of sleep-related breathing disorders
INVENTOR(S): Radulovacki, Miodrag; Carley, David W.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943319	A1	19990902	WO 1999-US4347	19990226
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2321900	AA	19990902	CA 1999-2321900	1999D226
EP 1066036	A1	20010110	EP 1999-909664	19990226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002504510	T2	20020212	JP 2000-533116	19990226
US 6331536	B1	20011218	US 2000-622823	20000823
US 2002086870	A1	20020704	US 2001-16901	2D011214

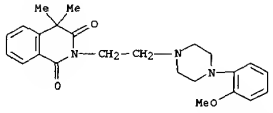
PRIORITY APPLN. INFO.: US 1998-76216P P 19980227
WO 1999-US4347 W 19990226
US 2000-622823 A1 20000823

AB Pharmacol. methods are provided for the prevention or amelioration of sleep-related breathing disorders via administration of agents or combinations of agents that possess serotonin-related pharmacol. activity.

IT **67339-62-2**, ARC239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agents, and combinations thereof, with serotonin-related activity for treatment of sleep-related breathing disorders)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

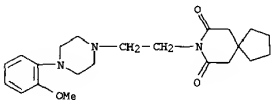
L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:547948 CAPLUS
DOCUMENT NUMBER: 131:281021
TITLE: Effect of several 5-hydroxytryptaminelA receptor ligands on the micturition reflex in rats: comparison with WAY 100635
AUTHOR(S): Testa, R.; Guarneri, L.; Poggesi, E.; Angelico, P.; Velasco, C.; Ibba, M.; Cilia, A.; Motta, G.; Riva, C.; Leonardi, A.
CORPORATE SOURCE: Pharmaceutical Research and Development Division, Milan, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(3), 1258-1269
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several novel N-arylpiperazine derivs. were synthesized and tested for their (1) affinity and functional activity on 5-hydroxytryptaminelA (5-HT1A) receptors in vitro; (2) activity in models predictive of antagonism at somatodendritic and postsynaptic 5-HT1A receptors; (3) and effects on the micturition reflex in anesthetized and conscious rats. These studies also included 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl] piperazine hydrobromide (NAN 190), B-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7, 9-dione dihydrochloride (BMY 7378), and N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-pyridinyl)cyclohexanecarboxamide (WAY 100635). Almost all compds. were found to be potent and selective for the human recombinant 5-HT1A receptor, with Ki values in the nanomolar range. [35S]GTP.gamma.S binding in HeLa cells expressing the recombinant human 5-HT1A receptor allowed classification of the compds. into neutral antagonists and partial agonists. Almost all neutral antagonists were active in blocking 8-hydroxy-2-dipropylaminotetralin (8-OH-DPAT)-induced forepaw treading in rats (postsynaptic model) and hypothermia in mice (somatodendritic model) with the same potency, whereas compds. showing partial agonistic activity were active in the postsynaptic model but were inactive, or poorly active, in the somatodendritic model. Neutral antagonists potently inhibited vol.-induced bladder-voiding contractions in anesthetized rats. Contractions were completely blocked, and the disappearance of bladder

L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
contractions lasted 7 to 13 min after the highest doses tested. Furthermore, neutral antagonists increased bladder vol. capacity in conscious rats during continuous transvesical cystometry, whereas micturition pressure was only slightly, and not dose-dependently, reduced.
Partial agonists were inactive or poorly active, inducing a disappearance time of bladder contractions that did not exceed 6 min in anesthetized rats, and failing to increase bladder vol. capacity in conscious rats. These findings indicate that only neutral 5-HT1A receptor antagonists are endowed with inhibitory effects on the bladder.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(N-arylpiperazine derivs. affinity at 5-HT1A receptor and other G protein-coupled receptors and effects 5-HT1A receptor ligands on micturition reflex in rats)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

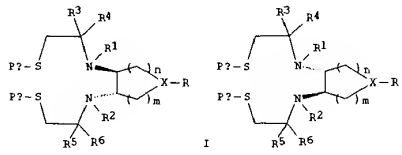
L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:528991 CAPLUS
DOCUMENT NUMBER: 131:153032
TITLE: Preparation of diaminedithiol stereoselective ligands
to complex with technetium-99m pertechnetate for use
as radioimaging agents
INVENTOR(S): Kung, Hank F.; Kung, Mei-ping; Zhuang, Zhi-ping
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940882	A2	19990819	WO 1999-US2513	19990205
WO 9940882	A3	19991104		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-73957P P 19980206
US 1998-78052P P 19980316
OTHER SOURCE(S): MARPAT 131:153032
GI



L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

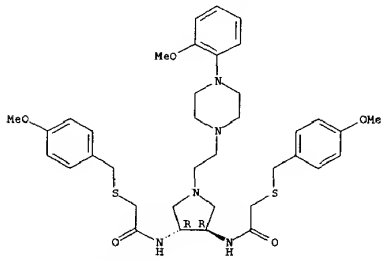
AB The present invention concerns novel diaminedithiol pyrrolidine deriv. ligands, represented by Formulas I and II, that form complexes with a radioactive metal through a chelate bond. The complexes are useful in radiodiagnostic compns. employed for imaging. In said ligand formulas, X = N or CH, R1 and R2 are selected from H or (un)substituted alkyl or aralkyl where at least one of R1 and R2 is H, R3 and R4 are H or together form a keto group, R5 and R6 are H or together form a keto group, m and n are independently 1 or 2, R = H, (un)substituted C1-6 alkyl, C3-7 cycloalkyl, or C6-10ar(C1-4)alkyl, and Pa = sulfur protecting group or H. In addn., R in the formulas above may be -L-B where L is a linking group, e.g., alkyl, amido, hydrazino, etc., and B is a targeting group, e.g., amino acid, peptide, protein, antibody, nucleic acid, steroid, lipid, saccharide, or cell membrane ligand. Radionuclide complexes of I and II are claimed, e.g., with Tc-99m, Re-186, and Re-188. The compds. of the invention avoid the formation of diastereomer mixts. based on incorporating [TcVO]+3N2S2 as a chelating moiety since these compds. form only one isomer when complexed with [99mTcVO4]+. A process for radioimaging with the radionuclide complexes and a kit for forming an injectable radiopharmaceutical compn. contg. I and II are claimed. Examples are provided for the prepn. of the stereoselective ligands, e.g., (3R,4R)-I (X = N, R = PhCH2, Pa = R1 = R2 = R3 = R4 = H, n = m = 1), its radiolabeling with [99mTc]pertechnetate, and its biodistribution in rats, which showed good heart uptake.

IT **235098-39-2P 235098-40-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for prepn. of chiral diaminedithiol pyrrolidine deriv. as chelate ligand with radionuclides used as radioimaging agents)

RN 235098-39-2 CAPLUS
CN Acetamide,
N,N'-[(3R,4R)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,4-pyrrolidinediyl]bis[2-[[(4-methoxyphenyl)methyl]thio]- (9CI) (CA INDEX NAME)

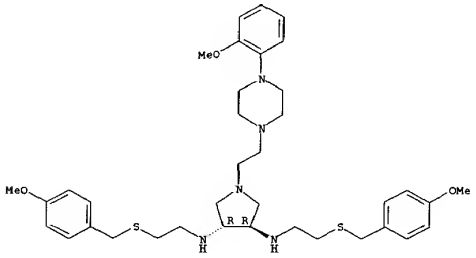
Absolute stereochemistry.

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 235098-40-5 CAPLUS
CN 3,4-Pyrrolidinediamine,
N,N'-bis[2-[[(4-methoxyphenyl)methyl]thio]ethyl]-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (3R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

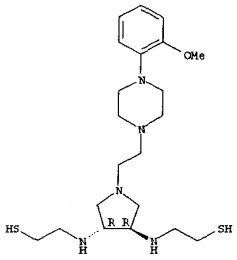


IT **235098-41-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(prepn. as chelate ligand with radionuclides used as radioimaging agents)

RN 235098-41-6 CAPLUS
CN Ethanethiol,
2,2'-[[(3R,4R)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,4-pyrrolidinediyl]diimino]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

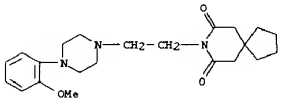


L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:494795 CAPLUS
DOCUMENT NUMBER: 131:295533
TITLE: Importance of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate
AUTHOR(S): McGrath, J. C.; Naghadeh, M. A.; Pediani, J. D.; Mackenzie, J. F.; Daly, C. J.
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neurosciences and Biomedical Systems, and Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK
SOURCE: European Urology (1999), 36(Suppl. 1), 80-88
CODEN: EUURAV; ISSN: 0302-2838
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB .alpha.-Adrenoceptor blocker drugs are commonly used in the clin. (non-surgical) treatment of BPH. .alpha.1-Adrenoceptors were originally sub-divided using agonists but, subsequently, were sub-divided using only antagonists in ligand-ligand interactions, which did not require agonists at all. Ultimately, proof that adrenoceptors are functional receptors for the natural ligands, noradrenaline and adrenaline, requires that agonists be used. The earlier excitement engendered by finding varying agonist potency series in different tissues has not been revisited to place it in the context of current concepts of .alpha.1-adrenoceptor subtypes. This review will consider the advantages and limitations of different agonists for the study of .alpha.1-adrenoceptor subtypes including "extreme" examples where the archetypal .alpha.1-adrenoceptor agonist phenylephrine activates .alpha.2-adrenoceptors and others where UK14304, often the .alpha.2-adrenoceptor agonist of choice, activates .alpha.1-adrenoceptors. New work will also be presented showing the interaction between agonists and the fluorescent .alpha.1-adrenoceptor antagonist QAPB. This introduces the novel point of view of studying the displacement of antagonists by agonists. Possible errors in antagonist classification arising from complexity in the actions of agonists and the recently developed method of fluorescent ligand binding on isolated living human prostatic smooth muscle cells will be discussed.

IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(importance of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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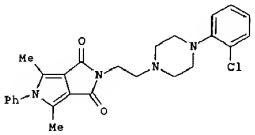
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:470679 CAPLUS
DOCUMENT NUMBER: 131:228607
TITLE: Synthesis and pharmacological screening of some N-(4-substituted-piperazin-1-ylalkyl)-3,4-pyrroledicarboximides
AUTHOR(S): Malinka, Wieslaw; Sieklucka-Dziuba, Maria; Rajtar, Grazyna; Rubaj, Andrzej; Kleinrok, Zdzislaw
CORPORATE SOURCE: Department of Chemistry of Drugs, Wroclaw University of Medicine, Wroclaw, 50-137, Pol.
SOURCE: Farmaco (1999), 54(6), 390-401
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:228607
GI

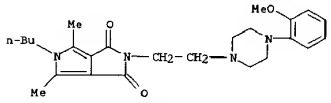


I

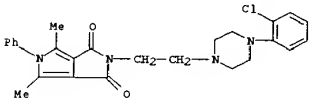
AB The synthesis and pharmacol. investigation of a new series of derivs. of pyrrole-3,4-dicarboximide, e.g. I, possessing the 4-substituted-piperazin-1-ylalkyl group linked to the imide nitrogen is presented. The products were evaluated for acute toxicity, and effectiveness in a series of CNS and arterial blood pressure tests. The preliminary pharmacol. screening was detd. in animal models. Several compds. demonstrated moderate to high analgesic activity in the "writhing syndrome" test (5f-1/60 LD50). Some of the structure-activity relationships are also discussed.

IT **244006-90-4P 244006-92-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)

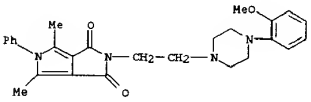
L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 244006-90-4 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



RN 244006-92-6 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)

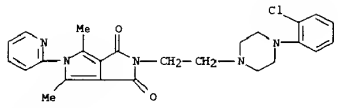


IT **244006-91-5P 244006-93-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)
RN 244006-91-5 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 244006-93-7 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)

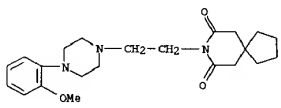
L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:449795 CAPLUS
DOCUMENT NUMBER: 131:223799
TITLE: Analysis of .alpha.1-adrenoceptor subtypes in rabbit
aorta and arteries: regional difference and co-existence
AUTHOR(S): Satoh, Mitsutoshi; Enomoto, Keisuke; Takayanagi, Issei; Koike, Katsuo
CORPORATE SOURCE: Department of Chemical Pharmacology, Toho University
School of Pharmaceutical Sciences, Funabashi, Japan
SOURCE: European Journal of Pharmacology (1999), 374(2), 229-240
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was done to det. the .alpha.1-adrenoceptor subtypes and to characterize the functional role of .alpha.1D-adrenoceptors in the following rabbit arteries: thoracic and abdominal aorta, mesenteric, renal and iliac arteries. In all arteries, selective .alpha.1D-adrenoceptor antagonist BMY 7378 dose dependently shifted the concn.-response curves for norepinephrine to the right. Schild plots of the results obtained from the inhibition by BMY 7378 for norepinephrine yielded a straight line with a slope of unity in thoracic (pA2 6.54) and abdominal (pA2 6.73) aorta. Slopes of Schild plots obtained from the inhibition by BMY 7378 for norepinephrine were significantly different from unity in mesenteric, renal and iliac arteries. Slopes of Schild plots for BMY 7378 were not different from unity in chloroethylclonidine-treated thoracic (pA2 6.49) and abdominal (pA2 6.61) aorta. Slopes of Schild plots for BMY 7378 were significantly different from unity in chloroethylclonidine-treated mesenteric, renal and iliac arteries. On the other hand, in Ca2+-free physiol. saline soln. (Ca2+-free PSS) slopes obtained from Schild plots for BMY 7378 were not different from unity in thoracic (pA2 6.41) and abdominal (pA2 6.28) aorta and mesenteric (pA2 6.55), renal (pA2 6.24) and iliac (pA2 6.64) arteries. BMY 7378 inhibited [3H]prazosin binding to thoracic (pKi 6.44) and abdominal (pKi 6.59) aorta with low potency, and mesenteric (pKi High 8.66, pKi Low 6.34), renal (pKi High 8.71, pKi Low 6.45) and iliac artery (pKi High 8.60, pKi Low 6.56). These results suggest that .alpha.1D-adrenoceptors play a significant role for contractile responses in renal and iliac artery, but play virtually no role in thoracic and abdominal aorta and that an .alpha.1-adrenoceptor subtype, which is pharmacol. distinguishable from the .alpha.1A-,

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
.alpha.1B- and .alpha.1D-adrenoceptor subtype, may co-exist in mesenteric artery.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor subtype pharmacol. characterization in rabbit aorta and arteries and regional differences and co-existence therein)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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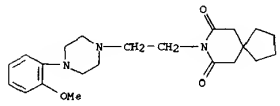
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:437513 CAPLUS
DOCUMENT NUMBER: 131:194652
TITLE: Microphysiometric analysis of human .alpha.1a-adrenoceptor expressed in Chinese hamster ovary cells
AUTHOR(S): Taniguchi, Takanobu; Inagaki, Rika; Murata, Satoshi; Akiba, Isamu; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: British Journal of Pharmacology (1999), 127(4), 962-968
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human recombinant .alpha.1a-adrenoceptor (AR) has been stably expressed in Chinese hamster ovary cells. Four stable clones, aH4, aH5, aH6 and aH7, expressing 30, 370, 940 and 2900 fmol AR mg-1 protein, resp., have been employed to characterize this AR subtype using radioligand binding and microphysiometry to measure extracellular acidification rates. Noradrenaline (NA) gave concn.-dependent responses in microphysiometry with increasing extracellular acidification rates. The potency of NA increased as the receptor d. increased; pEC50 values of NA for the clones aH4, aH5, aH6 and aH7 were 6.9, 7.5, 7.8 and 8.1, resp. This increase of potency according to receptor d. indicates the presence of spare receptor for NA. Methoxamine, phenylephrine, oxymetazoline and clonidine also gave concn.-dependent responses with various intrinsic activities. Antagonists shifted concn.-response curves for NA rightward in a concn.-dependent manner. Schild anal. revealed that the affinity profile of this AR subtype to antagonists in the clone aH7 had a typical pattern for the .alpha.1a-AR; high affinity for prazosin and WB 4101, and low affinity for BMY 7378 (pA2=9.5, 9.8 and 7.3, resp.). This profile is similar in the case of the clone aH4. These affinities were in good agreement with those obtained in binding expts. These results have demonstrated that (1) classical receptor theory can be applied in microphysiometry, and (2) microphysiometry is a useful tool to investigate the pharmacol. characterization of .alpha.1a-AR.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(microphysiometry in pharmacol. characterization of human

L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
.alpha.1a-adrenoceptor expressed in Chinese hamster ovary cells)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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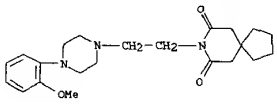
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and expression in vascular smooth muscle cell line cloned from p53 knockout mice)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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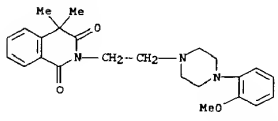
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:385955 CAPLUS
DOCUMENT NUMBER: 131:139836
TITLE: Characterization of .alpha.1-adrenoceptors expressed
in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53LMAC01 (AC01) cells
AUTHOR(S): Ohmi, Kazuhiro; Shinoura, Hitomi; Nakayama, Yasuhisa;
Goda, Nobuhito; Tsujimoto, Gozoh
CORPORATE SOURCE: Department of Pathology, National Children's Medicel
Research Center, Tokyo, 154-8509, Japan
SOURCE: British Journal of Pharmacology (1999), 127(3), 756-762
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We pharmacol. studied the .alpha.1-adrenoceptor (AR) subtype(s) involved
in receptor-mediated signeling in a novel vascular smooth muscle cell line
cloned from p53 knockout mice, P53LMAC01 (AC01) cells. Redioligend binding studies with [125I]-HEAT showed the existence of e homogeneous population of binding site with an affinity (Kd value) of 0.4 nM and a max. no. of binding sites (Bmax) of 100 fmol mg-1 protein. Catecholamines
competed for [125I]-HEAT binding stereospecifically and with the characteristic .alpha.1-AR potency series. Displacement curves for BMY-7378 and KMD-3213 best fitted a one-site model with a pKi value (-log10 (equil. inhibition const.)) of 6.06 and 7.07, resp. Reverse transcription-polymerase chain reaction (RT-PCR) assay detected .alpha.1B-
and .alpha.1D-AR, but not .alpha.1A-AR transcript. Chlorethylclonidine
(CEC) treatment nearly abolished (-)noradrenaline (NA) (10 .mu.M)-induced
inositol[1,4,5]trisphosphate (IP3) prodn., and BMY-7378 inhibited the response with a Ki value of 0.3 nM, which value was similar to that obtained in the cells expressing .alpha.1D-AR. In both AC01 cells and cells expressing .alpha.1D-AR, BMY-7378 protected .alpha.1-ARs from CEC
alkylation while it had little protective effect on CEC alkylation and NA-induced IP3 prodn. in cells expressing .alpha.1B-AR. The results indicate that AC01 cells contain predominantly .alphe.1B-ARs and e small
population of .alpha.1D-ARs; however, phosphoinositide (PI)/Ca2+ signaling
is mainly mediated through the minor population of .alpha.1D-ARs, rather
than the .alpha.1B-ARs.
IT **21102-95-4**, BMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor subtype functional pharmacol. characterization

L14 ANSWER 68 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:363284 CAPLUS
DOCUMENT NUMBER: 131:111771
TITLE: Functional .alpha.2C-adrenoceptors in human neuroblastoma SH-SY5Y cells
AUTHOR(S): Parsley, Stephanie; Gazi, Lucien; Bobirnac, Ionel; Loetscher, Erika; Schoeffter, Philippe
CORPORATE SOURCE: Nervous System Therapeutic Area, Novartis Pharma Research, Basel, CH-4002, Switz.
SOURCE: European Journal of Pharmacology (1999), 372(1), 109-115
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.2-adrenoceptor mediating inhibition of forskolin-stimulated cAMP accumulation in human neuroblastoma SH-SY5Y cells was further characterized. The .alpha.2-adrenoceptor agonists, UK 14,304 (5-bromo-6-(2-imidazolin-2-ylamino)quinoxaline), oxymetazoline, guanfacine, (-)-noradrenaline and clonidine concn.-dependently decreased
cAMP accumulation in this cell line (Emax .apprx.50% inhibition). Agonist
pEC50 values ranged between 6.7 and 7.8. Clonidine was a partiel agonist.
The effects of UK 14,304 were blocked after a pertussis toxin treatment.
The concn.-response curves of UK 14,304 were shifted to the right in a parallel manner by the following antagonists (mean pKB values): yohimbine
(8.17), idazoxan (7.63), prazosin (6.66), 2-[2-(4-(2-methoxyphenyl)piperazin-1-yl)ethyl]-4,4-dimethyl-1,3-(2H,4H) isoquinolindione (ARC 239; 7.12) end 2-(2,6-dimethoxyphenoxyethyl)aminomet
hyl-1,4-benzodioxane (WB-4101; 8.12). The relatively high pKB values of
prazosin and ARC 239 point to a non-.alpha.2A-adrenoceptor-mediated effect. The relatively high pKB value of WB-4101 further characterizes
the .alpha.2-adrenoceptor in SH-SY5Y cells as being of the .alpha.2C subtype. The anel. of the expression of .alpha.2-adrenoceptor subtypes by
reverse transcriptase-polymerase chain reaction (RT-PCR) revealed the exclusive presence of .alpha.2C-adrenoceptor mRNA in SH-SY5Y cells. The
authors propose that inhibition of forskolin-stimuleted cAMP accumulation
in SH-SY5Y cells be used as a functional model of human, native .alpha.2C-adrenoceptors.
IT **67339-62-2**, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(.alpha.2C-adrenoceptors characterization in human neuroblestoma SH-SY5Y cell by .alphe.2-adrenoceptor agonist and antagonist)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 68 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:282212 CAPLUS
DOCUMENT NUMBER: 130:311818
TITLE: Preparation of arylpiperazines as serotonin reuptake
inhibitors and 5-HT1D.alpha. antagonists
INVENTOR(S): Walker, Clint Duane; Wong, David Taiwai; Xu, Yao-Chang
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

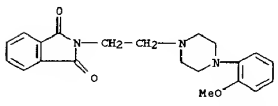
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920621	A1	19990429	WO 1998-US22265	19981021
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2307114	AA	19990429	CA 1998-2307114	19981021
AU 9911931	A1	19990510	AU 1999-11931	19981021
EP 1028958	A1	20000823	EP 1998-955031	19981021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2001520225	T2	20011030	JP 2000-516963	19981021
US 6342498	B1	20020129	US 2000-509957	20000331

PRIORITY APPLN. INFO.: US 1997-63493P P 19971022
WO 1998-US22265 W 19981021
OTHER SOURCE(S): MARPAT 130:311818
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl; Y = CO, CH2; Z = NH, C(COR), CH2; R = alkyl, cycloalkyl; n, m = 1-3] and their salts, serotonin reuptake inhibitors and 5-HT1D.alpha. receptor

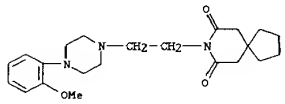
L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
antagonists useful in the treatment of depression and anxiety, were prepd.
and formulated. E.g., a 4-step synthesis of piperazine II, starting with 1-(2-methoxyphenyl)piperazine, was given. Representative compds. I showed
Ki at the 5-HT1A and 5-HT1D.alpha. receptors of at least 300 .mu.M.
IT **99718-67-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of arylpiperazines as serotonin reuptake inhibitors and 5-HT1D.alpha. antagonists)
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:203816 CAPLUS
DOCUMENT NUMBER: 131:27831
TITLE: New .alpha.1-adrenoceptor antagonist, JTH-601, shows more than 10 times higher affinity for human prostates than arteries
AUTHOR(S): Takahashi, Masahiko; Taniguchi, Takanobu; Murata, Satoshi; Okada, Kenichiro; Moriyama, Nobuo; Yamazaki, Satoru; Muramatsu, Ikunobu
CORPORATE SOURCE: Departments of Pharmacology and Urology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: Journal of Urology (Baltimore) (1999), 161(4), 1350-1354
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors compared the affinities of a new .alpha.1-adrenoceptor (AR) antagonist, JTH-601 with those of several .alpha.1-AR antagonists in human prostates and arteries. In the functional study, noradrenaline produced concn.-dependent contractions in human prostates and mesenteric arteries.
The pA2/pKB values for the antagonists in the human prostate were 9.78 for tamsulosin, 8.84 for JTH-601, 8.39 for WB4101, 8.23 for prazosin, 8.12 for JTH-601-G1 (a main metabolite of JTH-601 in human) and 6.57 for BMY7378.
Compared these affinities with those in the mesenteric artery, only JTH-601 and JTH-601-G1 exhibited unique uroselectivity, showing 10- to 20-fold higher affinity for the human prostate than for mesenteric artery.
The affinity profile of these antagonists suggested that the noradrenaline induced contractions in the human prostate and the mesenteric artery were mediated by the .alpha.1L-AR and .alpha.1B-AR, resp. In the competition binding study, the pharmacol. profiles of the antagonists against [3H]-prazosin were examd. in the human prostate and aorta. The resulting pKi values for JTH-601 and JTH-601-G1 were also approx. 10- to 20-fold higher for the human prostate than for the human aorta. These results have suggested that JTH-601 and JTH-601-G1 are unique uroselective .alpha.1-AR antagonists that show higher affinity for the human prostate than for the human arteries.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor antagonist JTH-601 affinity comparison with those of several .alpha.1-AR antagonists for human prostates and arteries)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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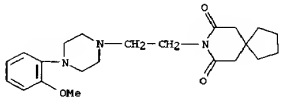
L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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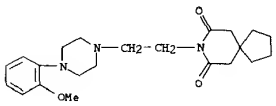
L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:186984 CAPLUS
DOCUMENT NUMBER: 131:30042
TITLE: Differences of antagonism for a selective .alpha.1D-adrenoceptor antagonist BMY 7378 in the rabbit thoracic aorta and iliac artery
AUTHOR(S): Satoh, Mitsutoshi; Enomoto, Keisuke; Takayanagi, Issei; Koike, Katsuo
CORPORATE SOURCE: Department of Chemical Pharmacology, Toho University
School of Pharmaceutical Sciences, Chiba, 274-8510,
Japan
SOURCE: Journal of Smooth Muscle Research (1998), 34(4), 151-158
CODEN: JSMRE2; ISSN: 0916-8737
PUBLISHER: Japanese Society of Smooth Muscle Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Based on the affinity of .alpha.1D-adrenoceptor subtype for a selective antagonist BMY 7378, we studied its functional role in rabbit thoracic aorta and iliac artery, and evaluated the subtypes of the .alpha.1-adrenoceptors that are activated by phenylephrine (a full agonist) and tizanidine (a partial agonist). In thoracic aorta, the concn.-response curves of phenylephrine and tizanidine were antagonized by BMY 7378 with low potency (pA2 values 6.68.+-.0.06 and 6.67.+-.0.06, slopes of Schild plot 1.06.+-.0.04 and 1.01.+-.0.04, resp.). On the other hand, in iliac artery concn.-response curves for phenylephrine were potently antagonized by a low concn. of BMY 7378, and the slope (0.75.+-.0.02) of the Schild plot was significantly different from unity. In iliac artery, a concn.-response curve of tizanidine was antagonized by BMY 7378 with low potency (pA2 value 6.64.+-.0.08, slope of Schild plot 1.01.+-.0.05). These results suggest that an .alpha.1D-adrenoceptor subtype contributes to .alpha.1-adrenoceptor mediating muscle contraction in iliac artery, but not in thoracic aorta of rabbit, and that it is activated by a full agonist phenylephrine but not by a partial agonist tizanidine.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antagonism difference for selective .alpha.1D-adrenoceptor antagonist BMY 7378 in thoracic aorta and iliac artery)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:127244 CAPLUS
DOCUMENT NUMBER: 131:13770
TITLE: Modification of sexual behavior of Long-Evans male rats by drugs acting on the 5-HT1A receptor
AUTHOR(S): Rehman, Jamil; Kaynan, Ayal; Christ, George; Valcic,
Mira; Maayani, Saul; Melman, Arnold
CORPORATE SOURCE: Department of Urology, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, 10467,
USA
SOURCE: Brain Research (1999), 821(2), 414-425
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Modulation of the sexual behavior of male rats by the anxiolytic buspirone (S-20499) and its analog gepirone were compared to the effects of 8-OH-DPAT (or DPAT, a selective 5-HT1A ref. agonist), and BMY-7378 (a selective 5-HT1A partial agonist). Long-Evans rats were used; modulation of copulatory behavior and alteration of penile reflexes were examd. Modulation of copulatory behavior was assessed by three indexes: frequency and length of intromission, and latency of ejaculation. DPAT, at doses of 1-8 mg/kg, reduced these three indexes in a time dependent manner such that the effects peaked at 45 min and normalized at 90 min. The dose-effect relation (assessed 45 min after DPAT injection) is bell-shaped with an ED50 approx. 1 mg/kg on the ascending limb of the curve. The effects of buspirone (2 mg/kg) and gepirone (2 mg/kg) on copulatory behavior were indistinguishable from control. BMY-7378 alone and in combination with these other 5-HT1A agonists reduced copulatory behavior, though not statistically significant. Penile reflexes, including no. of erections, cups and flips, were inhibited by these agents: DPAT>buspirone>gepirone (inactive at 2 mg/kg). Furthermore, the latency period to erection was at least doubled by DPAT (2 mg/kg). Buspirone and gepirone, however, reduced the latency period to erection. BMY-7378 inhibited penile reflexes when administered alone and even more in combination with DPAT or buspirone. Two butyrophenone analogs, spiperone (a 5-HT1A and dopamine D2 antagonist) and haloperidol (a D2 antagonist), were also tested for their interaction with DPAT. Both of these drugs (at 0.25 mg/kg, 60 min after administration) reduced all indexes of penile reflexes and copulation. Furthermore, in combination with DPAT (2 mg/kg, 45 min), the effects were synergistic such that sexual activity came nearly to a standstill. These opposing effects on putatively brain

L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
originated copulatory behavior and spinal mediated penile reflexes indicate that the effects of buspirone and DPAT on sexual behavior in the
male rat may be possible at different parts of the central nervous system.
If a tentative shared target site by DPAT and buspirone is the 5-HT1A receptor, than the same 5-HT receptor sub-type at different locations (brain, raphe nuclei, spinal cord and autonomic ganglia) may modulate rat
sexual behavior in opposing ways.
IT **21102-95-4**, BMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(modification of sexual behavior of Long-Evans male rats by drugs acting on the 5-HT1A receptor)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS
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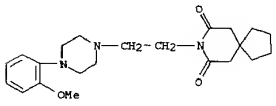
L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:120349 CAPLUS
DOCUMENT NUMBER: 130:277169
TITLE: Modulation of basal intracellular calcium by inverse
agonists and phorbol myristate acetate in rat-1 fibroblasts stably expressing
.alpha.1d-adrenoceptors
AUTHOR(S): Garcia-Sainz, J. Adolfo; Torres-Padilla, Maria Elena
CORPORATE SOURCE: Instituto de Fisiologia Celular, Universidad Nacional
autonoma de Mexico, Mexico City, 04510, Mex.
SOURCE: FEBS Letters (1999), 443(3), 277-281
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rat-1 fibroblasts stably expressing .alpha.1d-adrenoceptors, BMY 7378,
phentolamine, chloroethylclonidine and 5-methylurapidil decreased basal
[Ca2+]i. WB 4101 induced a very small effect on this parameter but when
added before the other antagonists it blocked their effect. All these agents inhibited the action of norepinephrine. Phorbol myristate acetate
also blocked the effect of norepinephrine and decreased basal [Ca2+]i. Staurosporine inhibited these effects of the phorbol ester. Our results
suggest that: (1) .alpha.1d-adrenoceptors exhibit spontaneous ligand-independent activity, (2) BMY 7378, phentolamine, chloroethylclonidine and 5-methylurapidil act as inverse agonists and (3)
protein kinase C activation blocks spontaneous and agonist-stimulated .alpha.1d-adrenoceptor activity.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(inverse agonist and protein kinase C modulation of intracellular calcium in rat-1 fibroblasts stably expressing .alpha.1d-adrenoceptors)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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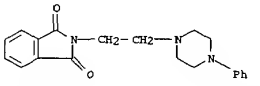
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 74 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:68279 CAPLUS
DOCUMENT NUMBER: 130:291449
TITLE: Affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides
AUTHOR(S): Andronati, S. A.; Voronina, T. A.; Sava, V. M.; Molodavkin, G. M.; Makan, S. Yu.; Soboleva, S. G.
CORPORATE SOURCE: A.V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Odessa, 270080, Ukraine
SOURCE: Molecular Recognition and Inclusion, Proceedings of
the International Symposium on Molecular Recognition
and Inclusion, 9th, Lyon, Sept. 7-12, 1996 (1998), Meeting Date 1996, 245-249. Editor(s): Coleman, Annette W. Kluwer: Dordrecht, Neth.
CODEN: 67FSAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors report here affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides.
IT **75000-24-7**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(affinity for both 5-HT1A- and D1-receptors and anxiolytic activity of
N-(arylpiperazinylalkyl)-phthalimides)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



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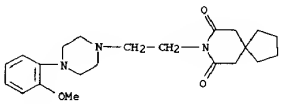
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:55960 CAPLUS
DOCUMENT NUMBER: 130:262474
TITLE: Ultrasonic vocalizations in rat pups: effects of serotonergic ligands
AUTHOR(S): Olivier, B.; Molewijk, H. E.; Van Der Heyden, J. A.
M.; Van Oorschot, R.; Ronken, E.; Mos, J.; Miczek, K.
A.
CORPORATE SOURCE: Department of CNS Pharmacology, Solvay Pharmaceuticals, Weesp, 1380 DA, Neth.
SOURCE: Neuroscience and Biobehavioral Reviews (1998), 23(2),
215-227
CODEN: NBREDE; ISSN: 0149-7634
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ligands with varying intrinsic activity and selectivity for the various
subtypes of the serotonin receptor were tested in the rat pup ultrasonic
vocalization (USV) model, a putative animal model reflecting anxiety. USV
were elicited by isolating rat pups from their mother and littermates by
placing them on a warm (37.degree.) or a cold (18.degree.) plate.
Concurrently, the neg. geotaxic (NG) response and rectal temp. were detd.
to assess the potentially sedative and hypothermic effects of putative
anxiolytics. USV were reduced at low doses and in both temp. conditions
by the full 5-HT1A receptor agonists flesinoxan and 8-OH-DPAT-HBr and the
partial 5-HT1A receptor agonists buspirone, ipsapirone and BMY 7378. The
5-HT1A receptor antagonists NAN-190, (.+-.)-WAY 100135, and (S)-UH-301
reduced USV at higher doses and only in one of both test conditions. The
selective 5-HT1A receptor antagonist DU 125530 did not influence USV at
the cold plate up to high doses, although concomitantly the neg. geotaxis
was disturbed. The neg. geotaxis was impaired after all 5-HT1A receptor
ligands, except BMY 7378 and (.+-.)-WAY 100135. Hypothermia coincided
with USV-suppression, except for NAN-190 and (S)-UH-301. The
USV-suppressing action of flesinoxan (3 mg/kg) could be antagonized by DU
125530, but not its NG effect. However, the hypothermia induced by
flesinoxan was antagonized by DU 125530. USV were also suppressed by the
5-HT uptake inhibitors fluvoxamine (both warm and cold plate) and

L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
clomipramine (only warm plate). The tricyclic antidepressant imipramine
only decreased USV on the cold plate, however, in a U-shaped dose-response
curve. At the highest dose tested, no decrease was present. The 5-HT
uptake stimulant tianeptine reduced USV under both conditions.
Fluvoxamine had no side effects, clomipramine induced hypothermia and
tianeptine clearly had sedative properties. The 5-HT1B/2C receptor
agonist TFMPP (trifluorometaphenylpiperazine) stimulated USV at a low dose
at the cold plate and suppressed USV at a high dose under both conditions.
The 5-HT2A/2C receptor antagonist ketanserin enhanced USV at low doses
under both conditions and had no effect at a higher dose. Concurrently
heavy sedation and hypothermia occurred. The 5-HT3 receptor agonist
phenylbiguanide and the 5-HT3 receptor antagonist ondansetron had no
effect in this paradigm. Clearly, subtypes of the 5-HT receptor affect
rat pup USV differentially.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(serotonin receptor subtype ligand differential effect on ultrasonic
vocalization in rat pup)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

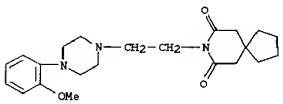


●2 HCl

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:53147 CAPLUS
DOCUMENT NUMBER: 130:247298
TITLE: Characterization of 5-HT1A receptor functional coupling in cells expressing the human 5-HT1A receptor
as assessed with the cytosensor microphysiometer
AUTHOR(S): Dunlop, John; Zhang, Yingxin; Smith, Deborah L.; Schechter, Lee E.
CORPORATE SOURCE: Wyeth-Ayerst Research, CNS Disorders, Princeton, NJ,
08543, USA
SOURCE: Journal of Pharmacological and Toxicological Methods
(1998), 40(1), 47-55
CODEN: JPTMEZ; ISSN: 1056-8719
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The functional activity of a series of 5-HT1A receptor ligands has been
evaluated in a cell line expressing the human 5-HT1A receptor (h5-HT1A
.cntdot. CHO) using the agonist-stimulated increase in extracellular
acidification rate, measured with the microphysiometer, as a functional
assay. Both 5-CT and 8-OH-DPAT were potent agonists in stimulating an
increase in extracellular acidification rate in h5-HT1A .cntdot. CHO cells
with estd. EC50 values of 1.2 and 7.8 nM, resp. Addnl., these two 5-HT1A
receptor agonists elicited a similar max. response. Concn.-dependent
agonist activity was also obsd. in the presence of buspirone, ipsapirone,
BMY 7378, NAN-190 and WAY 100135, and each of these compds. behaved as
partial 5-HT1A receptor agonists. The selective 5-HT1A receptor
antagonist WAY 100635 produced a potent (IC50, 2.3 nM) and complete block
of the 8-OH-DPAT-stimulated response. An evaluation of the inhibitory
activity of a series of 5-HT1A receptor antagonists produced the following
rank order of potency: WAY 100635 > LY 206130 (IC50, 7.1 nM) > WAY 100135
(30.8 nM) > pindolol (76.2 nM) > (-)UH-301 (92.8 nM). Parallel studies on
the inhibition of forskolin-stimulated adenylyl cyclase activity in
h5-HT1A .cntdot. CHO cells revealed that agonist potencies were generally
similar between the two functional assays and were in good agreement with
the estd. 5-HT1A receptor binding affinities. However, the relative
efficacies detd. for the partial agonists in the cAMP assay were
substantially greater than those obsd. with the microphysiometer.
Finally, antagonists were considerably weaker in the cAMP assay compared

L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
with the microphysiometer. The evaluation of 5-HT1A ligands using the microphysiometer, which represents a very distinct indice of 5-HT1A receptor function compared with the cAMP assay, results in a different profile of functional activity.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(5-HT1A receptor functional coupling characterization in cells expressing the human 5-HT1A receptor as assessed by extracellular acidification rate detn. with the cytosensor microphysiometer and cAMP
formation)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS

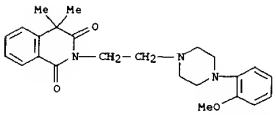
ACCESSION NUMBER: 1999:32567 CAPLUS
DOCUMENT NUMBER: 130:76506
TITLE: Role of the third intracellular loop of the alpha-2 adrenergic receptor in regulating receptor density
AUTHOR(S): Heck, Donald A.; Bylund, David B.
CORPORATE SOURCE: Dep. Pharmacology, Medical Center, Univ. Nebraska, Omaha, NE, 68198, USA
SOURCE: Pharmacology Reviews and Communications (1998), 10(2), 101-110
CODEN: PHRCF6
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It was previously shown that the mechanism of down-regulation of .alpha.-2 adrenergic receptor subtypes is an increase in the rate const. for receptor disappearance. In addn., subtype-specific differences were found in the regulation of receptor d. in the presence of norepinephrine. For example, blocking functional G protein coupling with pertussis toxin alters the time-course of norepinephrine-induced down-regulation for .alpha.-2A receptors while having little effect on the time-course of receptor down-regulation for .alpha.-2B receptors. In contrast, treatment with pertussis toxin alone decreases .alpha.-2B receptor d. while having little effect on .alpha.-2A receptor d. To explore these subtype-specific differences, a chimeric receptor was constructed in which the 3rd intracellular loop of the .alpha.-2B receptor was replaced with the 3rd intracellular loop of the .alpha.-2A receptor. It was found that the chimeric receptor exhibits similar characteristics to the wild-type receptor in terms of radioligand binding, potency of norepinephrine to down-regulate receptor d., and effects of pertussis toxin on receptor d. In contrast, replacement of the 3rd intracellular loop of the .alpha.-2B receptor with that of the .alpha.-2A receptor alters the regulation of receptor d. in both the absence and presence of norepinephrine.

IT **67339-62-2**, ARC-239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(affinity for .alpha.-2 adrenergic receptors and chimeric receptor)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:804830 CAPLUS
DOCUMENT NUMBER: 130:191412
TITLE: Synthesis and Structure-Activity Relationships of a New Model of Arylpiperazines. 4.1-[.omega.-(4-Arylpiperazin-1-yl)alkyl]-3-(diphenylmethylene)-2,5-pyrrolidinediones and -3-(9H-fluoren-9-ylidene)-2,5-pyrrolidinediones: Study of the Steric Requirements of the Terminal Amide Fragment on 5-HT1A Affinity/Selectivity
AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose; Rovat, Tandu K.; Fernandez, Esther; Vicente, Bruno; Sanz, Antonio M.; Hernandez, Medardo; Orensanz, Luis
CORPORATE SOURCE: Departamento de Quimica Organica I Facultad de Ciencias Quimicas, Universidad Complutense, Madrid, 28040, Spain
SOURCE: Journal of Medicinal Chemistry (1999), 42(1), 36-49
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:191412

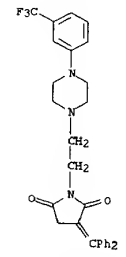
AB In the present paper, the authors report the synthesis and the binding profile on 5-HT1A, .alpha.1 and D2 receptors of a new series of 1-[.omega.-(4-arylpiperazin-1-yl)alkyl]-3-(diphenylmethylene)-2,5-pyrrolidinediones (I) (1-4) and -3-(9H-fluoren-9-ylidene)-2,5-pyrrolidinediones (II) (1-4), in which the alkyl linker contains 1-4 methylenes and the aryl group is variously substituted. The results obtained are compared to those previously reported for bicyclohydantoin and the related bicyclic amine series. A considerable part of the tested compds. demonstrated moderate to high affinity for 5-HT1A and .alpha.1 receptor binding sites but had no affinity for D2 receptors. The study of the length of the alkyl chain and the imide substructure has allowed the authors to suggest some differences between the 5-HT1A and the .alpha.1-adrenergic receptors: (i) for I and II, affinity for the 5-HT1A receptor as a function of the length of the methylene linker decreases in the order 4>1 .mchgt. 3.apprx.2, while for the .alpha.1 receptor affinity decreases in the order 3.apprx.4 > 1.apprx.2; (ii) the no-pharmacophoric steric pocket (receptor zone which does not hold the pharmacophore of the

L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

ligand but holds a nonessential fragment of the mol.) in the 5-HT1A receptor has less restriction than the corresponding pocket in the .alpha.1 receptor. Compds. which are highly selective for .alpha.1-adrenergic receptors displayed antagonist activity. The best compromise between affinity and selectivity for 5-HT1A receptors is reached in these new series with n = 1, which is in agreement with the authors previous results for the bicyclohydantoin derivs. Two selected compds. retain agonist properties at postsynaptic 5-HT1A receptors. The same 5-HT1A agonist profile found in these compds. suggests the existence of two different no-pharmacophoric steric pockets in this receptor and a different interaction of compds. with n = 1 and n = 4. The information obtained from the interpretation of the energy minimization and 2D-NOESY expts. of these compds. together with the synthesis and binding data of new conformationally restrained analogs is in good agreement with this working hypothesis.

IT **220798-79-8P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(synthesis and structure-activity relationships of a new model of arylpiperazines and study of steric requirements of terminal amide fragment on 5-HT1A affinity/selectivity in relation to .alpha.1-adrenergic and D2 receptors)

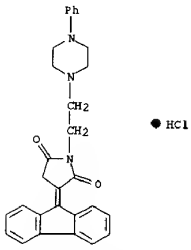
RN 220798-79-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

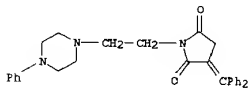
IT **193287-12-6P 193287-13-7P 193287-15-9P**
193287-16-0P 193287-18-2P 193287-19-3P
220798-76-5P 220798-85-6P 220798-90-3P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
(Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC
(Process)
(synthesis and structure-activity relationships of a new model of arylpiperazines and study of steric requirements of terminal amide fragment on 5-HT1A affinity/selectivity in relation to .alpha.1-adrenergic and D2 receptors)

RN 193287-12-6 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



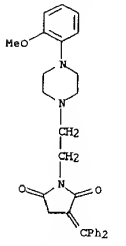
● HCl

RN 193287-13-7 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



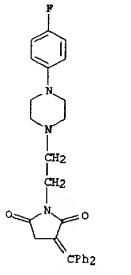
●2 HCl

RN 193287-15-9 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



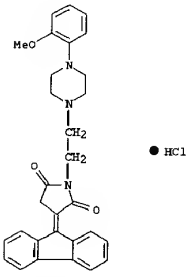
●2 HCl

RN 193287-16-0 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



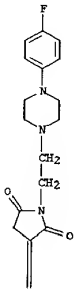
●2 HCl

RN 193287-18-2 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



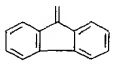
● HCl

RN 193287-19-3 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



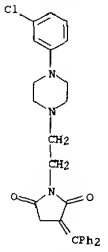
L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A



● HCl

RN 220798-76-5 CAPLUS
CN 2,5-Pyrrolidinedione,
1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-
(diphenylmethylene)-, dihydrochloride (9CI) (CA INDEX NAME)

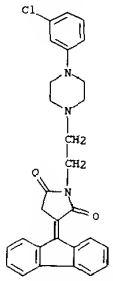


●2 HCl

RN 220798-85-6 CAPLUS
CN 2,5-Pyrrolidinedione,
1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-(9H-
fluoren-9-ylidene)-, monohydrochloride (9CI) (CA INDEX NAME)

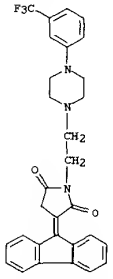
L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 220798-90-3 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-[3-
(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride
(9CI)
(CA INDEX NAME)



● HCl

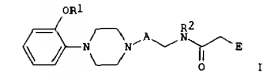
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR
THIS

L14 ANSWER 79 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:764277 CAPLUS
DOCUMENT NUMBER: 130:24968
TITLE: Preparation of aryl-substituted piperazines
useful in
the treatment of benign prostatic hyperplasia
INVENTOR(S): Jolliffe, Linda; Murray, William; Pulito,
Virginia;
Reitz, Alan; Li, Kiaobing; Mulcahy, Linda;
Maryanoff,
Cynthia; Villani, Frank
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851298	A1	19981119	WO 1998-US9023	19980508
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,				
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,				
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,				
VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,				
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				
CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9873669	A1	19981208	AU 1998-73669	19980508
EP 984777	A1	20000315	EP 1998-920950	19980508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, FI, RO				
US 6071915	A	20000606	US 1998-74789	19980508
BR 9809804	A	20000627	BR 1998-9804	19980508
JP 2002511065	T2	20020409	JP 1998-549276	19980508
ZA 9803968	A	19991111	ZA 1998-3968	19980511
NO 9905518	A	20000111	NO 1999-5518	19991111
US 6303594	B1	20011016	US 2000-526224	20000315

PRIORITY APPLN. INFO.: US 1997-46236P P 19970512
US 1998-74789 A1 19980508
WO 1998-US9023 W 19980508
OTHER SOURCE(S): MARPAT 130:24968
GI

L14 ANSWER 79 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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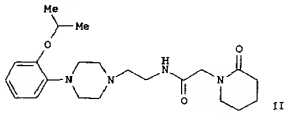


II

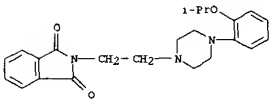
AB The title compds. [I; A = (CH2)n; R1 = H, C1-6 alkyl, (un)substituted Ph, substituted phenyl(C1-5 alkyl); R2 = H, C1-6 alkyl, C1-5 alkenyl, C1-5 alkynyl, (un)substituted phenyl(C1-5 alkyl); E = piperidino, phthalimido, etc.; n = 1-6] and their pharmaceutically acceptable salts, .alpha.-1A adrenergic receptor antagonists useful for the therapy of benign prostatic hyperplasia, were prepd. Pharmaceutical compns. contg. I and intermediates used in their manuf. are also claimed. For example, hydrazinolysis of 1-(2-phthalimidoethyl)-4-(2-isopropoxyphenyl)piperazine with MeNHNH2 gave 1-(2-aminoethyl)-4-[2-(2-isopropoxy)phenyl]piperazine which was amidated with 1-carboxymethyl-2-piperidone (prepn. by N-alkylation of .delta.-valerolactone with BrCH2CO2CMe3 followed by ester hydrolysis given) to give II. This (as citrate salt) had IC50 8.7 nmol for binding on .alpha.1a receptor subtype cloned with poly(A)+ RNA from human hypocampus and prostate tissue.

IT **216252-67-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrazinolysis; prepn. of aryl-substituted piperazines as .alpha.-1A adrenoceptor antagonists for therapy of benign prostatic hyperplasia)

RN 216252-67-4 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-[2-(1-methylethoxy)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 79 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 80 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:727766 CAPLUS

DOCUMENT NUMBER: 130:90774

TITLE: .alpha.1D-Adrenoceptors contribute to the neurogenic vasopressor response in pithed rats

AUTHOR(S): Castillo, E. F.; Lopez, R. M.; Rodriguez-Silverio, J.; Bobadilla, R. A.; Castillo, C.

CORPORATE SOURCE: Seccion de Estudios de Posgrado e Investigacion, Escuela Superior de Medicina del IPN, Plan de San Luis y Diaz Miron, Casco de Sto Tomas, Mexico, 17, Mex.

SOURCE: Fundamental & Clinical Pharmacology (1998), 12(6), 584-589
CODEN: FCPHEZ; ISSN: 0767-3981

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

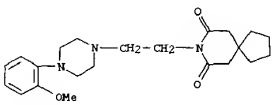
AB The aim of the present study was to assess the role of vascular .alpha.1D-adrenoceptors in the sympathetic vasopressor response in vivo. Specifically, we evaluated the effect of a selective .alpha.1D-adrenoceptor antagonist, BMY 7378 (8-(2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl-8-azaspiro(4,5)decane-7,9-dione 2HCl)), on the vasopressor response induced by preganglionic (T7-T9) sympathetic stimulation in the pithed rat. The vasopressor response was dose-dependently sensitive to inhibition by i.v. BMY 7378 (0.1, 0.31, 1 and 3.1 mg/kg), doses of 1 and 3.1 mg/kg being equally effective. Like BMY 7378, 5-methylurapidil (0.1, 0.31, 1 and 3.1 mg/kg) antagonized the vasopressor response to spinal stimulation; doses of 1 and 3.1 mg/kg were also equally effective. In combination expts., BMY 7378 (1 mg/kg, i.v.) and the .alpha.1A-adrenoceptor antagonist, 5-methylurapidil (1 mg/kg, i.v.), showed an additive effect. The present results demonstrate that the .alpha.1D-adrenoceptor subtype plays an important role in the pressor response to sympathetic nerve stimulation in the pithed rat, and confirm the participation of the .alpha.1A-adrenoceptor subtype in the same response.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1D-adrenoceptors contribute to the neurogenic vasopressor response in pithed rats)

RN 21102-95-4 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

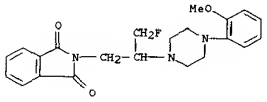
L14 ANSWER 80 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

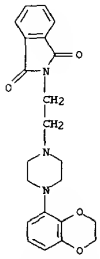
L14 ANSWER 81 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:713718 CAPLUS
DOCUMENT NUMBER: 130:52388
TITLE: Studies on quinazoline IX. Fluorination versus 1,2-migration in the reaction of 1,3-bifunctionalized amino-2-propanol with DAST
AUTHOR(S): Chern, Ji-Wang; Chang, Jun-Yi; Usifoh, Cyril O.; Gutsait, Alexander
CORPORATE SOURCE: Sch. Pharmacy, Coll. Medicine, National Taiwan Univ., Taipei, Taiwan
SOURCE: Tetrahedron Letters (1998), 39(46), 8483-8486
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:52388
AB Treatment of 1-phthaloylamino-3-[4-(2-methoxyphenyl)piperazin-1-yl]propanol with diethylaminosulfur trifluoride (DAST) induced 1,2-migration via a proposed spiroaziridinium intermediate to give N-[2-fluoro-3-[4-(2-methoxyphenyl)piperazin-1-yl]propyl]phthalimide in 13% yield and N-[2-fluoromethyl-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]phthalimide in 73% yield.
IT **217170-74-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorination vs. 1,2-migration in reaction of 1,3-bifunctionalized amino-2-propanol with DAST)
RN 217170-74-6 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[3-fluoro-2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:660055 CAPLUS
DOCUMENT NUMBER: 130:3828
TITLE: Functional characteristics of a series of N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines as 5-HT1A receptor ligands. Structure-activity relationships
AUTHOR(S): Van Steen, B. J.; Van Wijngaarden, I.; Ronken, E.; Soudijn, W.
CORPORATE SOURCE: Solvay Pharmaceuticals Research Laboratories, Weesp, 1380, Neth.
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(18), 2457-2462
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The agonistic/antagonistic profile of a series of 10 N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines is evaluated in the in vitro adenylyl cyclase assay. The profile is severely affected by the characteristics of the N4-substituents ranging from full agonism (benzamidoethyl deriv.), mixed agonism/antagonism (phthalimidobutyl deriv.) to predominantly antagonism (saccharinbutyl derivate). A novel full antagonist, as potent as WAY 100635, is obtained by substitution of Cl at C-7 of the benzodioxinyl moiety in the saccharinbutyl derivate.
IT **171877-07-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship of of (benzodioxinyl)piperazines as 5-HT1A receptor ligands)
RN 171877-07-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

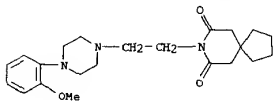
L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

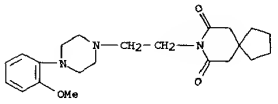
L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:508546 CAPLUS
DOCUMENT NUMBER: 129:211986
TITLE: .alpha.1L-adrenoceptors in canine pulmonary artery
AUTHOR(S): Flavahan, N. A.; Hales, M. A.; Aleskowitch, T. D.; Gaine, S. P.; Vanhoutee, P. M.
CORPORATE SOURCE: Department of Medicine, Johns Hopkins University, Baltimore, MD, USA
SOURCE: Journal of Cardiovascular Pharmacology (1998), 32(2), 308-316
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to characterize the .alpha.1-adrenoceptors of the canine pulmonary artery. Arterial rings from lower lung lobes were suspended for isometric-tension recording in the presence of cocaine (5 .times. 10-6 M), hydrocortisone (3 .times. 10-5 M), propranolol (5 .times. 10-6 M), and rauwolscine (10-7 M) to inhibit neuronal uptake, extraneuronal uptake, and .beta.- and .alpha.2-adrenoceptors, resp. Prazosin was more potent against contractions evoked by phenylephrine (pA2 of 9.7) compared with methoxamine (pA2 of 8.4). SZL49 (10-8 and 3 .times. 10-8 M), an irreversible .alpha.1-adrenergic antagonist, inhibited responses to phenylephrine but not methoxamine. With norepinephrine, low concns. of prazosin (3 .times. 10-10 M and 10-9 M) caused inhibition of the concn.-response curve; a higher concn. (3 .times. 10-9 M) failed to produce further inhibition, whereas increasing the concn. of the antagonist (to 10-8 and 3 .times. 10-8 M) caused further rightward shifts in the concn.-response curve. The Arunlakshana and Schild plot revealed two components corresponding to pA2 values of 9.8 and 8.4. After SZL49 (3 .times. 10-8 M), the Arunlakshana and Schild plot for the interaction between norepinephrine and prazosin was linear and generated a pA2 of 8.3. Contractions evoked by phenylephrine were inhibited by the .alpha.1B/.alpha.1D-adrenoceptor antagonist, chloroethylclonidine (10-5 M), or by the .alpha.1B-antagonist, risperidone (pA2 value of 8.5), but were relatively resistant to inhibition by the selective .alpha.1D-antagonist, BMY7378 (-log KB of 6.1). The results suggest that two .alpha.1-adrenoceptor subtypes mediate contraction of the canine pulmonary artery. One subtype has high affinity for prazosin (.alpha.1H,

L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
likely to be .alpha.1B), is activated by phenylephrine, and is inhibited
by SZL49. The other subtype has lower affinity for prazosin (.alpha.1L),
is stimulated by methoxamine, and is relatively resistant to SZL49. The
physiol. agonist, norepinephrine, causes contraction by activating both
subtypes.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BUU (Biological use, unclassified); BIOL (Biological
study); USES (Uses)
(.alpha.1L-adrenoceptors in canine pulmonary artery)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:401962 CAPLUS
DOCUMENT NUMBER: 129:130877
TITLE: Search for .alpha.1-adrenoceptor subtypes selective antagonists: design, synthesis and biological activity of cystazosin, an .alpha.1D-adrenoceptor antagonist
AUTHOR(S): Minarini, Anna; Budriesi, Roberta; Chiarini, Alberto; Leonardi, Amedeo; Melchiorre, Carlo
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, I-40126, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(11), 1353-1358
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:130877
AB Two novel quinazolines related to both prazosin and its open analog were synthesized, and their biol. profile at .alpha.1-adrenoceptor subtypes was assessed by functional assays in rat isolated tissues, namely prostatic vas deferens (.alpha.1A), spleen (.alpha.1B) and aorta (.alpha.1D). Furthermore, the binding profile of cystazosin was assessed at native .alpha.2 and D2 receptors, and cloned human 5-HT1A receptors, in comparison to prazosin, (+)-cyclazosin, the prazosin open analog and BMY 7383. It turned out that the cystamine-bearing quinazoline (cystazosin) has a reversed affinity profile relative to (+)-cyclazosin owing to a higher affinity for .alpha.1D-adrenoceptors and a significantly lower affinity for the .alpha.1A and .alpha.1B subtypes. Furthermore, in comparison to BMY 7378, cystazosin displays a much better specificity profile since it has lower affinity for D2 and 5-HT1A receptors.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(search for .alpha.1-adrenoceptor subtype-selective antagonists by design and synthesis and biol. activity of cystazosin)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

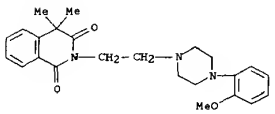
L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:386654 CAPLUS
DOCUMENT NUMBER: 129:131120
TITLE: Effects of imidazoline derivatives on cholinergic motility in guinea-pig ileum: involvement of presynaptic .alpha.2-adrenoceptors or imidazoline receptors?
AUTHOR(S): Colucci, Rocchina; Blandizzi, Corrado; Carignani, Diego; Placanica, Giorgio; Lazzeri, Gloria; Del Tacca, Mario
CORPORATE SOURCE: Department of Oncology, Division of Pharmacology and Chemotherapy, University of Pisa, Via Roma 55, Pisa, I-56126, Italy
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1998), 357(6), 682-691
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigates the possibility that imidazoline receptors mediate modulation of cholinergic motor functions of the guinea-pig ileum. For this purpose, the effects of a series of compds. with known affinity for .alpha.2-adrenoceptors and/or imidazoline recognition sites were exam. on the cholinergic twitch contractions evoked by elec. field stimulation (0.1 Hz) of longitudinal muscle-myenteric plexus prepns. Addnl. expts. were carried out on ileal strips preincubated with [3H]choline, superfused with physiol. salt soln. contg. hemicholinium-3, and subjected to elec. field stimulation (1 Hz). The stimulation-induced outflow of radioactivity was taken as an index of endogenous acetylcholine release. .alpha.-Methyl-noradrenaline, noradrenaline, clonidine, medetomidine, oxymetazoline and xylazine caused a concn.-dependent inhibition of twitch responses (IC50 from 0.13 to 1.05 .mu.M; Emax from 85.9 to 92.5%). Rilmenidine and agmatine were less potent in reducing the twitch activity, and the latter compd. acted also with low intrinsic activity (IC50=44.9 .mu.M; Emax=35.5%). In interaction expts., the inhibitory action of clonidine on twitch responses was competitively antagonized by RX 821002 [2-(2-methoxy-1,4-benzodioxan-2-yl)-2-imidazoline], idazoxan, rauwolscine, yohimbine and BRL 44408 {2-[2H-(1-methyl-1,3-dihydroisoindole)-methyl]-4,5-dihydroimidazoline}, whereas prazosin (10 .mu.M), ARC 239 [2-(2,4-(o-methoxyphenyl)-piperazin-1-yl)ethyl-4,4-dimethyl-1,3-(2H,4H)-isoquinolindione; 10 .mu.M] and BRL 41992 [1,2-dimethyl-2,3,9,13b-tetrahydro-1H-dibenzo[c,f]imidazol[1,5-a]azepine; 10 .mu.M] were without effect. Rauwolscine antagonized the

L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
inhibitory effects of various agonists on ileal twitch activity in a competitive manner and with similar potency. Agmatine and idazoxan did not significantly modify the twitch contractions when tested in the presence of .alpha.2-adrenoceptor blockade by rauwolscine (3 .mu.M) or RX 821002 (1 .mu.M). Linear regression anal. showed that the affinity values of antagonists correlated with their affinity at the .alpha.2A and .alpha.2D binding sites as well as at previously classified .alpha.2A/Dadrenoceptor subtypes, whereas no significant correlation was obtained when comparing tha potency ests. of agonists and antagonists with the affinity at I1 or I2 binding sites. When tested on the elec. induced outflow of tritium, .alpha.-methyl-noradrenaline, noradrenaline, clonidine, medetomidine, oxymetazoline, xylazine and rilmenidine yielded inhibitory concn.-response curves which were shifted rightward to a similar extent in the presence of rauwolscine (3 .mu.M). In the absence of further drugs, agmatine significantly reduced tha evoked tritium outflow at the highest concns. tested (10 and 100 .mu.M), whereas idazoxan (up to 100 .mu.M) was without effect. When RX 821002 (1 .mu.M) was added to the superfusion medium, neither agmatine nor idazoxan modified the evoked outflow of radioactivity. The results argue against modulation by imidazoline receptors of acetylcholine release from myenteric plexus nerve terminals. They provide evidence that compds. endowed with imidazoline-like structures affect the cholinergic motor activity of the guinea-pig ileum by interacting with presynaptic .alpha.2-adrenoceptors belonging to the .alpha.2D subtype.

IT **67339-62-2**, AR-C 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(imidazoline deriv. effect on cholinergic motility in guinea-pig ileum in relation to involvement of presynaptic .alpha.2-adrenoceptors or imidazoline receptors)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



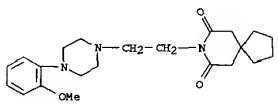
L14 ANSWER 86 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:349268 CAPLUS
DOCUMENT NUMBER: 129:62433
TITLE: Theoretical descriptors in quantitative structure-affinity and selectivity relationship study of potent N4-substituted arylpiperazine 5-HT1A receptor antagonists
AUTHOR(S): Menziani, M. C.; De Benedetti, P. G.; Karelson, M.
CORPORATE SOURCE: Dipartimento di Chimica, Universita' di Modena, Modena, 41100, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(5), 535-550
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of ad hoc defined size and shape descriptors and theor. descriptors derived on a single structure to give powerful interpretative and predictive QSAR models was compared and evaluated with respect to the quality of the pharmacol. data available for structurally diverse 5-HT1A receptor antagonists, displaying selectivity towards the .alpha.1-adrenergic receptor.

IT **21102-94-3**
RL: BAC (Biological activity or effector, except advarse); BSU (Biological study, unclassified); CAT (Catalyst use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic usa); BIOL (Biological study); PROC (Process); USES (Uses)
(theor. descriptors in QSAR study of arylpiperazine 5-HT1A receptor antagonists)

RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphanyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



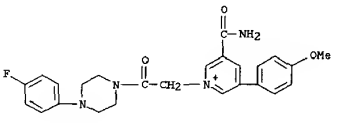
L14 ANSWER 87 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:348051 CAPLUS
DOCUMENT NUMBER: 129:81649
TITLE: Solid phase synthesis of a 1,3,5-trisubstituted pyridinium salt library
AUTHOR(S): Lago, M. Amparo; Nguyen, Thomas T.; Bhatnagar, Pradip
CORPORATE SOURCE: Medicinal Chemistry Department, SmithKline Beecham Pharmaceuticals, Colleville, PA, 19426-0989, USA
SOURCE: Tetrahedron Letters (1998), 39(23), 3885-3888
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:81649

AB The synthesis of a 1,3,5-trisubstituted pyridinium salt combinatorial array contg. two variable groups was accomplished in good yields. This entailed the incorporation of 5-bromonicotinic acid onto the resin, followed by Pd(0) catalyzed Suzuki coupling, then alkylation of the pyridine nitrogen and finally cleavage from the resin. A mix and split scheme was also carried out.

IT **209398-54-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of a trisubstituted pyridinium salt library)

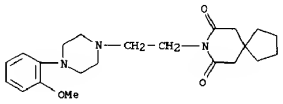
RN 209398-54-9 CAPLUS
CN Pyridinium, 3-(aminocarbonyl)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]-2-oxoethyl]-5-(4-methoxyphenyl)-, bromide (9CI) (CA INDEX NAME)



● Br^-

L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:319424 CAPLUS
DOCUMENT NUMBER: 129:63374
TITLE: Pharmacological and immunocytochemical characterization of subtypes of alpha-1 adrenoceptors in dog aorta
AUTHOR(S): Low, A. M.; Lu-Chao, H.; Wang, Y. F.; Brown, R. D.; Kwan, C. Y.; Daniel, E. E.
CORPORATE SOURCE: Department of Biomedical Sciences, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(2), 894-901
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, the effects of nine alpha-1 adrenoceptor antagonists [prazosin, WB 4101 (WB), chloroethylclonidine (CEC), 5-methylurapidil (5-MU), BMY 7378 (BMY), MDL 73005EF (MDL73), MDL 72832 (MDL72), RS 17053 (RS) and SK&F 105854 (SKF)] were studied on contractile responses to phenylephrine (PE) of the endothelium-denuded dog aorta in vitro. All antagonists, except CEC, 5-MU and RS, produced concn.-dependent competitive inhibition of contractile responses of the aorta to PE. The rightward shift of the concn.-response curves of PE yielded const. pKB values with increasing antagonist concns. in most cases allowing a single pooled value to be detd.: for prazosin, a pKB of 8.99.+-.0.11 (n = 20, KB of 1.03 nM); for WB, a pKB of 8.75.+-.0.08 (n = 23, KB of 1.76 nM); for BMY, a pKB of 7.21.+-.0.13 (n = 13, KB of 62 nM); for MDL72, a pKB of 7.95.+-.0.15 (n = 12, KB of 11.2 nM); and for SK&F 105854, a pKB of 5.82.+-.0.08 (n = 15, KB of 1.52 .mu.M). For MDL73, pKB values decreased with antagonist concn.: 7.88.+-.0.06 at 10 nM, 7.56.+-.0.28 at 100 nM and 6.92.+-.0.18 at 1000 nM, which suggests the presence of more than one receptor subtype. CEC (10 and 100 .mu.M) almost completely inhibited responses to PE; lower concns. had no significant effect. 5-MU (10-300 nM) and RS (3-300 nM) were ineffective antagonists in this tissue. Because WB, a highly selective alpha-1D and alpha-1A adrenoceptor subtypes inhibitor, blocked PE responses (with less affinity than for alpha-1A adrenoceptors), and 5-MU and RS, which are selective blockers for alpha-1A adrenoceptor, were ineffective, we conclude that alpha-1A adrenoceptors are absent in the dog aorta. The effects of the less selective MDL72 were

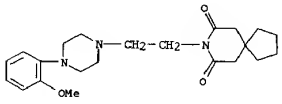
L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
inconsistent with actions at alpha-1B or alpha-1D adrenoceptors. Although WB shifted the PE concn.-response curve to the right, the abilities of BMY, MDL73 and SKF to inhibit competitively PE contraction were of lower affinity compared with expectations for interaction with alpha-1D adrenoceptors; they are not the predominant subtype. The complete inhibition of PE responses by CEC suggests that the dog aorta contains the alpha-1B adrenoceptor subtype. In immunocytochem. studies of the expression of alpha-1B adrenoceptor, all cells apparently expressed this protein. Moreover, Western blot studies of the microsomal fractions confirmed the presence of alpha-1B adrenoceptors. In the dog aorta, the alpha-1 adrenoceptors predominantly resemble alpha-1B rather than alpha-1D adrenoceptors as reported in the rat aorta.
IT **21102-95-4**, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. and immunocytochem. characterization of subtypes of alpha-1 adrenoceptors in dog aorta)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

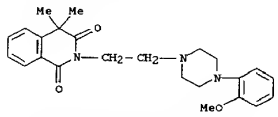
L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:304032 CAPLUS
DOCUMENT NUMBER: 129:62431
TITLE: Computer modeling of size and shape descriptors of .alpha.1-adrenergic receptor antagonists and quantitative structure-affinity/selectivity relationships
AUTHOR(S): Montorsi, Monia; Menziani, M. Cristina; Cocchi, Marina; Fanelli, Francesca; De Benedetti, Pier G.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena, 41100, Italy
SOURCE: Methods (Orlando, Florida) (1998), 14(3), 239-254
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Computational chem. and mol. modeling procedures allow the authors to define and compute ad hoc size and shape descriptors on the different prototropic forms assumed by drugs in biotest solns. Together with exptl. data measured on a well-identified target receptor, these descriptors are essential elements for obtaining simple, consistent, comparable, and easily interpretable theor. quant. structure-activity relation (QSAR) models based on the ligand similarity-target receptor complementarity paradigm. In this context, quant. size and shape affinity/subtype selectivity relationships have been modeled for a large set of very heterogeneous .alpha.1a-, .alpha.1b-, and .alpha.1d- adrenergic receptor antagonists. The linear QSAR models generated have been validated by predicting both binding affinity and selectivity of a test set of noncongeneric antagonists. The satisfactory results obtained highlight both the simplicity and the versatility of the approach presented.
IT **21102-95-4**, BMY 7378 **67339-62-2**, ARC 239
99718-67-9
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(computer modeling of size and shape descriptors of .alpha.1-adrenergic receptor antagonists and quant. structure-affinity/selectivity relationships)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

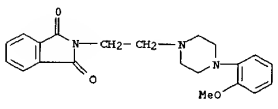


●2 HCl

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

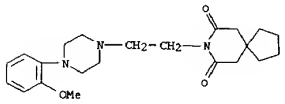


RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



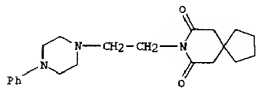
L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:285099 CAPLUS
DOCUMENT NUMBER: 129:63311
TITLE: Characterization of .alpha.1-adrenoceptor subtypes in the pig
AUTHOR(S): Wikberg-Matsson, Anna; Wikberg, Jarl E. S.; Uhlen, Staffan
CORPORATE SOURCE: Academic Hospital, Department of Ophthalmology, Uppsala University, Uppsala, Swed.
SOURCE: European Journal of Pharmacology (1998), 347(2/3), 301-309
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The identities of the .alpha.1-adrenoceptor subtypes present in various tissues of the pig were studied using [3H]prazosin radioligand binding. The subtypes were characterized by performing competition expts. for various subtype selective drugs. In the cerebral cortex, spleen and heart, both .alpha.1A- and .alpha.1B-adrenoceptors were detected. In the liver was found only the .alpha.1A-subtype, while in the aorta was found only the .alpha.1B-subtype. An .alpha.1-adrenoceptor subtype was present in the adrenal gland with a high affinity for prazosin, the pKd value being 9.6, but with relatively low affinities for other .alpha.1-adrenoceptor binding drugs. The adrenal gland .alpha.1-adrenoceptor did not seem to represent the classical .alpha.1D-subtype, since drugs selective for the .alpha.1D-subtype in other species, including BMY7378 and SKF104856, showed low affinities for the pig adrenal gland .alpha.1-adrenoceptor.
IT **21102-95-4**, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.1-adrenoceptor subtypes characterization in pig organs)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

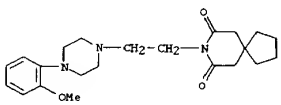


●2 HCl

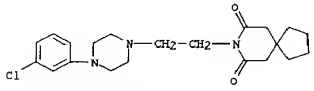
L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:254237 CAPLUS
DOCUMENT NUMBER: 129:22916
TITLE: Study of structure-activity relations in a series of buspirone analogs using an electron-topological approach
AUTHOR(S): Dimoglo, A. S.; Chumakov, Yu. M.; Simonov, Yu. A.; Andronati, S. A.; Bocelli, G.
CORPORATE SOURCE: Inst. Khim., AN Resp. Moldova, Chisinau, Moldova
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1998), 32(1), 36-40
CODEN: KHFZAN; ISSN: 0023-1134
PUBLISHER: Izdatel'stvo Folium
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The structure-related psychotropic activity of a series of buspirone analogs is described.
IT **21090-07-3 21102-94-3 21103-20-8 25024-93-5 25024-94-6 75000-28-1 83928-69-2 83928-77-2 83928-78-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-psychotropic activity relations in series of buspirone analogs: electron-topol. approach)
RN 21090-07-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



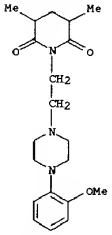
RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 21103-20-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

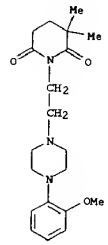


RN 25024-93-5 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

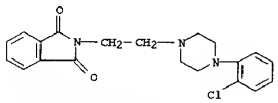


RN 25024-94-6 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

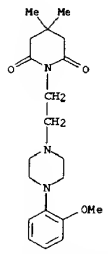


RN 75000-28-1 CAPLUS
CN 1M-Isoindole-1,3(2M)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

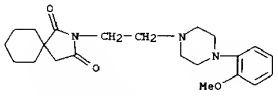


RN 83928-69-2 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

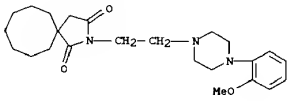
L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83928-77-2 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

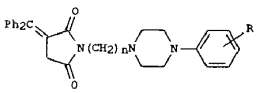


RN 83928-78-3 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:220189 CAPLUS
DOCUMENT NUMBER: 128:308471
TITLE: 1-[.omega.-(4-Arylpiperazin-1-yl)alkyl]-3-diphenylmethylene-2,5-pyrrolidinediones as 5-HT1A receptor ligands: study of the steric requirements of the terminal amide fragment on 5-HT1A affinity/selectivity
AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose; Rovat, Tandu K.; Fernandez, Esther; Sanz, Antonio M.; Orensanz, Luis
CORPORATE SOURCE: Department de Quimica Organica I, Fac. de Ciencias Quimicas, Univ. Complutense, Madrid, 28040, Spain
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(6), 581-586
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



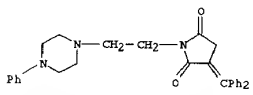
I

AB Title compds. I [n = 1-4; R = H, 2-OMe, 3-Cl, 3-CF3, 4-F] were prepd. from the maleimide, CH2O, and the piperazine or from the maleic anhydride and the aminoalkylpipearazine and their binding profiles for the 5-Ht1A, .alpha.1, and D2 receptors were evaluated. The study of the length of the alkyl chain and the imide substructure suggests some important differences between the non-pharmacophoric sites of both 5-HT1A and .alpha.-adrenergic receptors, which could be of great importance in designing new selective ligands.

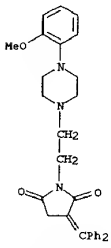
IT **206430-38-8P 206430-41-3P 206430-43-5P 206430-45-7P 206430-46-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(steric requirements of the terminal amide fragment of

L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
arylpiperazinylalkylpyrrolidinediones on 5-HT1A affinity/selectivity)

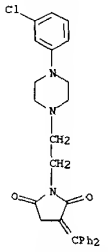
RN 206430-38-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



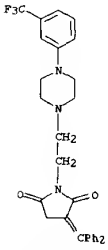
RN 206430-41-3 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



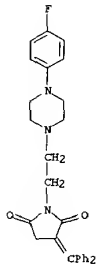
RN 206430-43-5 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-(diphenylmethylene)- (9CI) (CA INDEX NAME)



RN 206430-45-7 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 206430-46-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

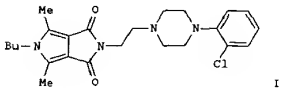


L14 ANSWER 93 OF 263 CAPLUS COPYRIGHT 2002 ACS

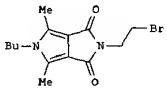
ACCESSION NUMBER: 1998:56192 CAPLUS
DOCUMENT NUMBER: 128:75420
TITLE: Preparation of novel derivative of pyrrole-3,4-dicarboxylic acid imide
INVENTOR(S): Malinka, Wieslaw; Kleinrok, Zdzislaw; Siekluckа, Maria
PATENT ASSIGNEE(S): Akademia Medyczna, Pol.
SOURCE: Pol., 4 pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 172418	B1	19970930	PL 1993-299531	19930701

GI



I



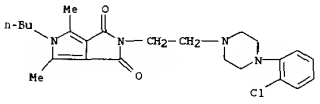
II

AB The title compd. I, useful as psychotropic, was prepd. by reacting the imide II with N-(2-chlorphenyl)piperazine in the presence of K2CO3 in MeCN. Compd. I reduced the spontaneous activity in mice at 1/80 LD50 (LD50 = 766.3).

IT **159658-13-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel deriv. of pyrrole-3,4-dicarboxylic acid imide)

RN 159658-13-6 CAPLUS

CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



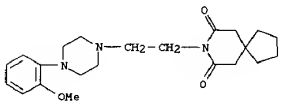
L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:53477 CAPLUS
DOCUMENT NUMBER: 128:200886
TITLE: Discriminative stimulus effects of 8-hydroxy-2-(di-n-propylamino)tetralin in pigeons and rats: species similarities and differences
AUTHOR(S): Kleven, Mark S.; Koek, Wouter
CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 284(1), 238-249
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study the authors examd. the effects of 5-HT1A ligands in rats trained to discriminate 0.16 mg/kg i.p. 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) from saline in a two-lever, fixed ratio (FR) 10 schedule of food reinforcement, and in pigeons trained to discriminate 0.31 mg/kg i.m. 8-OH-DPAT from saline in a two-key, FR30 schedule of food reinforcement. In both species, 8-OH-DPAT and a variety of structurally unrelated 5-HT1A ligands occasioned dose-related, relatively high levels of drug-appropriate selection (i.e: .gtoreq.67%). A significant pos. correlation was found between estd. ED50 values in both species (r = 0.84). Further, 5-HT1A antagonists, NAN-190, penbutolol, (-)-pindolol, tertatolol and WAY-100635, produced dose-related decreases in 8-OH-DPAT-appropriate selection, and their potencies for antagonism in rats and pigeons were highly correlated (r = 0.96). The potency of WAY 100635 in rats and pigeons was quantified by Schild anal. (apparent in vivo pA2 values: 7.8 vs. 8.3, rat vs. pigeon, resp.). Although most 5-HT1A agonists produced similar 8-OH-DPAT-like discriminative stimulus effects in both species, two compds., lisuride and eltoprazine, occasioned high levels of drug-appropriate selection in pigeons, but not in rats. In contrast, idazoxan, yohimbine, LEK 8804 and BMY 7378 produced greater effects in rats. Among this latter group of compds., only BMY 7378 blocked the discriminative stimulus effects of 8-OH-DPAT in pigeons, which suggested that intermediate levels of drug-appropriate selection obsd. with the remaining compds. are not necessarily the result of low intrinsic activity. Overall, these results demonstrate similarities in the

L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

discriminative stimulus effects of 8-OH-DPAT in rats and pigeons despite different training conditions (e.g., training dose and route of administration). Even so, the finding that some 5-HT1A ligands did not produce similar effects in rats and pigeons illustrates the need to examine possible 8-OH-DPAT-like discriminative stimulus effects of compds. in both species.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(discriminative stimulus effects of hydroxy(di-n-propylamino)tetralin in pigeons and rats in relation to species similarities and differences)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:9220 CAPLUS
DOCUMENT NUMBER: 128:110381
TITLE: Isoindol-1-one Analogs of 4-(2'-methoxyphenyl)-1-[2'-[N-(2''-pyridyl)-p-iodobenzamido]ethyl]piperazine (p-MPPI) as 5-HT1A Receptor Ligands
AUTHOR(S): Zhuang, Zhi-Ping; Kung, Mei-Ping; Mu, Mu; Kung, Hank F.
CORPORATE SOURCE: Departments of Radiology and Pharmacology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(2), 157-166
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

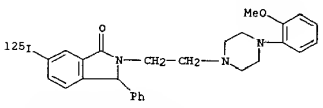
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In developing radioiodinated antagonists for in vivo imaging of 5-HT1A receptors with SPECT, a series of new arylpiperazine benzamido derivs., including I (p-MPPI) (Kd = 0.36 nM), as potential ligands for 5-HT1A receptors were reported previously. However, rapid in vivo metab. may have caused the breakdown of the amide bond of [123I]-I and rendered this agent obsolete as an in vivo imaging agent in humans. To improve the in vivo stability of I, a series of cyclized amide analogs were designed and synthesized. In vitro binding, metabolic stability, and in vivo biodistribution of these new derivs. were investigated. Several five-membered-ring isoindol-1-ones displayed very high in vitro binding affinity, esp. II (R = H, R1 = NO2; R = OH, R1 = iodo; R = H, R1 = iodo), which showed Ki values of 0.05, 0.65, and 0.07 nM, resp. The affinities for 5-HT1A receptors of other cyclized amide derivs. III (R2 = Br, iodo) and IV, were 1.09, 2.54, and 14.9 nM, resp. Compared to [125I]-I, iodinated cyclized amide derivs. [125I]-II (R = H, R1 = iodo) and [125I]-III (R2 = iodo) displayed a slower metab. in human liver microsomal and cytosolic prepns. Biodistribution of [125I]-II (R = H, R1 = iodo) and [125I]-III (R2 = iodo) in rats (after an i.v. injection) displayed moderate to low brain uptakes with little or no specific localization in

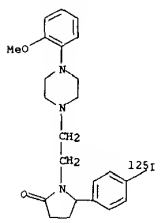
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

hippocampal region, where 5-HT1A receptors are concd. These data indicate that the new iodinated ligands showed high binding affinities and better metabolic stability but displayed unexpectedly low selective binding to 5-HT1A receptors in vivo. Addnl. structural modifications may be needed to correct the unfavorable properties displayed for these iodinated cyclized amide derivs. for in vivo biodistribution in rats.

IT **201531-46-6P 201531-47-7P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine isoindolone analogs as serotonin 5-HT1a receptor ligands)
RN 201531-46-6 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-6-(iodo-125I)-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

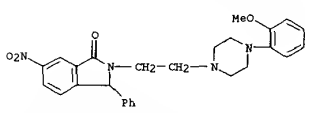


RN 201531-47-7 CAPLUS
CN 2-Pyrrolidinone, 5-[4-(iodo-125I)phenyl]-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

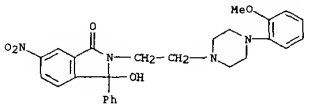


IT **201531-35-3P 201531-36-4P 201531-37-5P**
201531-40-0P 201531-42-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine
isoindolone analogs as serotonin 5-HT1a receptor ligands)

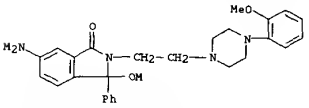
RN 201531-35-3 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



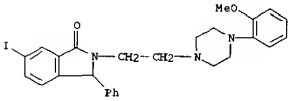
RN 201531-36-4 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



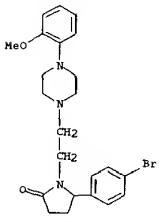
RN 201531-37-5 CAPLUS
CN 1H-Isoindol-1-one, 6-amino-2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 201531-40-0 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-6-iodo-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

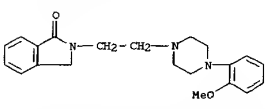


RN 201531-42-2 CAPLUS
CN 2-Pyrrolidinone, 5-(4-bromophenyl)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

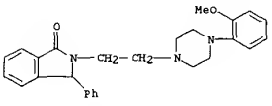


IT **99718-69-1P 201531-33-1P 201531-34-2P**
201531-38-6P 201531-39-7P 201531-41-1P
201531-44-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine
isoindolone analogs as serotonin 5-HT1a receptor ligands)

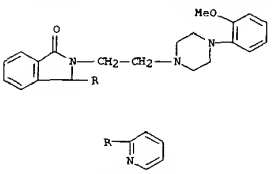
RN 99718-69-1 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



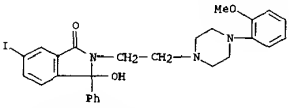
RN 201531-33-1 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 201531-34-2 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-(2-pyridinyl)- (9CI) (CA INDEX NAME)

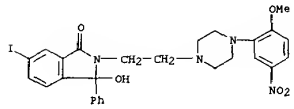


RN 201531-38-6 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

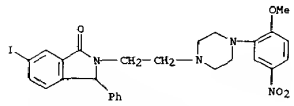


RN 201531-39-7 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-[4-(2-methoxy-5-nitrophenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

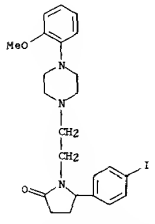
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 201531-41-1 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-6-iodo-2-[2-[4-(2-methoxy-5-nitrophenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 201531-44-4 CAPLUS
CN 2-Pyrrolidinone, 5-(4-iodophenyl)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

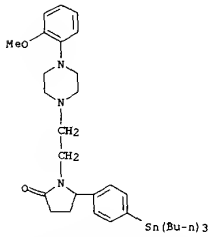


IT **201531-43-3P 201531-45-5P 201532-02-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (methoxyphenyl)[(pyridyl]iodobenzamidoethyl]piperazine

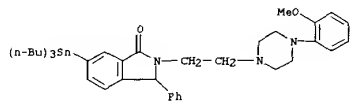
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
isoindolone analogs as serotonin 5-HT1a receptor ligands)

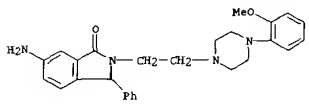
RN 201531-43-3 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5-[4-(tributylstannyl)phenyl]- (9CI) (CA INDEX NAME)



RN 201531-45-5 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl-6-(tributylstannyl)- (9CI) (CA INDEX NAME)



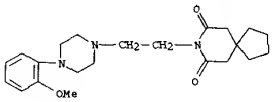
RN 201532-02-7 CAPLUS
CN 1H-Isoindol-1-one, 6-amino-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



L14 ANSWER 96 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:6089 CAPLUS
DOCUMENT NUMBER: 128:149828
TITLE: Pharmacological evidence for .alpha.1D-adrenoceptors in the rabbit ventricular myocardium: analysis with BMY 7378
AUTHOR(S): Yang, Tuang-Tian; Endoh, Masao
CORPORATE SOURCE: Department of Pharmacology, Yamagata University School of Medicine, Yamagata, 990-23, Japan
SOURCE: British Journal of Pharmacology (1997), 122(8), 1541-1550
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It was exam. by means of BMY 7378, a selective antagonist of .alpha.1D-adrenoceptors, whether .alpha.1D-adrenoceptors contribute to the regulation of myocardial contractility and hydrolysis of phosphoinositide (PI) in rabbit ventricular muscle. BMY 7378 had a biphasic antagonistic action on the pos. inotropic effect (PIE) of phenylephrine depending on the concn. BMY 7378 at 1-10 nM shifted the concn.-response curve (CRC) for the PIE of phenylephrine to the right and downward and at 100 nM to 1 .mu.M it antagonized the PIE in a competitive manner, the slope of Schild plot being 0.93 and the pA2 being 7.17.+-.0.09. The inhibitory action of BMY 7378 at 1-10 nM is ascribed to the selective action on .alpha.1-adrenoceptors because the PIE of neither isoprenaline nor endothelin-3 and angiotensin II was affected by this compd. over this concn. range. In the presence of 100 nM WB 4101, the antagonistic action of BMY 7378 at 1-10 nM remained unchanged but the antagonistic action of BMY 7378 at 100-300 nM disappeared. The antagonistic action of BMY 7378 at 1 nM was unaffected by 100 nM (+)-niguldipine. Following pretreatment with chloroethylclonidine, BMY 7378 at 1 nM inhibited the maximal response to phenylephrine but the pD2 value for phenylephrine was increased in the presence of BMY 7378. The CRC for phenylephrine was shifted to the left in the presence of 10-100 nM BMY 7378 but it was shifted to the right by BMY 7378 at 300 nM. Stimulation of PI hydrolysis induced by phenylephrine was not affected by BMY 7378 up to 10 nM but it was reduced significantly

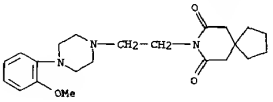
L14 ANSWER 96 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
by BMY 7378 at higher concns. (100 nM to 1 .mu.M). BMY 7378 inhibited the
[3H]prazosin specific binding to the rabbit ventricular membrane fraction
in a monophasic manner with a pKi value of 7.53.+-.0.09. The results indicate that in rabbit ventricular muscle, BMY 7378 at 1-10 nM suppressed
the maximal response to phenylephrine (probably mediated by .alpha.1D-adrenoceptors) and at 10-100 nM it inhibited the neg. inotropic
effect of phenylephrine, the mechanisms of which remain to be characterized. At higher concns. (100 nM to 1 .mu.M) BMY 7378 antagonized
the functional and biochem. response via a presumed interaction mainly
with the .alpha.1B-adrenoceptor and partially with the .alpha.1A-adrenoceptor.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(pharmacol. evidence for .alpha.1D-adrenoceptors in rabbit ventricular
myocardium using BMY 7378)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:749539 CAPLUS
DOCUMENT NUMBER: 128:44122
TITLE: Immunocytochemical localization of the alpha-1B adrenergic receptor and the contribution of this and
the other subtypes to vascular smooth muscle contraction: analysis with selective ligands and antisense oligonucleotides
AUTHOR(S): Piascik, Michael T.; Hrometz, Sandra L.; Edelmann, Stephanie E.; Guarino, Richard D.; Hadley, Robert W.;
Brown, R. Dale
CORPORATE SOURCE: Department of Pharmacology and Vascular Biology Research Group, University of Kentucky College of Medicine, Lexington, KY, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics
(1997), 283(2), 854-868
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The contribution of the alpha-1B adrenergic receptor (AR) to vascular smooth muscle contraction has been assessed using a combination of immunol., mol. biol. and pharmacol. approaches. A subtype-selective antibody detected alpha-1B immunoreactivity in the medial layer of the aorta, caudal, femoral, iliac, mesenteric resistance, renal and superior
mesenteric arteries. Receptor protection assays and antisense oligonucleotides were used to assess the contribution of the alpha-1B AR
to contraction. The alpha-1B AR was implicated in mediating the phenylephrine-induced contraction of the mesenteric resistance artery. The alpha-1D AR was implicated in mediating the contraction of the aorta,
femoral, iliac and superior mesenteric arteries. Similarly, the alpha-1A
AR was implicated in mediating contraction of the caudal and renal arteries. In vivo application of antisense oligonucleotides targeted to
the translational start site of the alpha-1B AR had no effect on the phenylephrine-induced contraction of the femoral or renal arteries. In
contrast, antisense oligonucleotides directed against the alpha-1D AR significantly inhibited the phenylephrine response in the femoral artery
but had no effect on the renal artery. Application of alpha-1A AR antisense oligonucleotides inhibited the contraction of the renal artery
without effect on the femoral artery. These data show that (1) alpha-1B
AR immunoreactivity is widely distributed in the same peripheral arteries
in which previous studies detected its mRNA, and (2) despite this distribution, receptor protection and antisense oligonucleotide studies

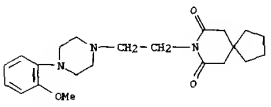
L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
indicate that the alpha-1B AR mediates the contraction of only the mesenteric resistance artery.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BUU (Biological use, unclassified); BIOL (Biological
study); USES (Uses)
(.alpha.-adrenergic receptor subtype localization and contribution to
vascular smooth muscle contraction)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 98 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:720998 CAPLUS
DOCUMENT NUMBER: 128:18934
TITLE: Investigation of .alpha.1-adrenoceptor subtypes mediating vasoconstriction in rabbit cutaneous resistance arteries
AUTHOR(S): Smith, K. M.; Macmillan, J. B.; McGrath, J. C.
CORPORATE SOURCE: Clinical Research Initiative in Heart Failure, Neuroscience and Biomedical Systems, University of Glasgow, Glasgow, G12 8QQ, UK
SOURCE: British Journal of Pharmacology (1997), 122(5), 825-832
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cutaneous resistance arteries (c.r.a.) (internal diam.=240.94.+-.5.42 .mu.m, n=67/25 (no. arteries/no. animals)) from New Zealand white rabbits
were mounted in wire myographs and a normalization procedure followed. Cumulative concn.-response curves (CCRCs) were constructed for the .alpha.-adrenoceptor agonists noradrenaline (NA), (R)A61603 and phenylephrine (PE) in the presence of cocaine (3 .mu.M), propranolol (1
.mu.M) and corticosterone (10 .mu.M). The effects of competitive .alpha.1-adrenoceptor antagonists, prazosin, WB4101, 5-methyl-urapidil,
HV723, BMY7378 and the irreversible .alpha.1B selective compd. chloroethylclonidine (CEC) were examd. vs. the potency and max. response
of the c.r.a.s to noradrenaline. The high potency of A-61603 relative to
PE has been shown to differentiate both functional and binding site .alpha.1A- or .alpha.1B-adrenoceptors from .alpha.1D-adrenoceptors: A-61603 was 944 times more potent than phenylephrine (at EC50) suggesting
the presence of a functional .alpha.1A or .alpha.1B as opposed to an .alpha.1D-subtype. Exposure to chloroethylclonidine (CEC; 100 .mu.M) decreased the max. response to noradrenaline but did not significantly change noradrenaline sensitivity indicating that a substantial part of noradrenaline-induced vasoconstriction in rabbit cutaneous arteries is CEC-insensitive. The potencies of prazosin (pA2 = 9.14) and WB4101 (pA2 =
9.30) indicate the involvement of prazosin-sensitive functional .alpha.1-adrenoceptors. The slopes of corresponding Schild plots for prazosin and WB4101 did not include neg. unity which implies the possible
involvement of more than one functional .alpha.1-adrenoceptor subtype in
noradrenaline-induced vasoconstriction in rabbit cutaneous resistance arteries. In contrast to this, in the case of 5-methyl-urapidil and HV723, the Schild plot slope parameters were not significantly different
from neg. unity over the range of concns. used; the low pA2 value for 5-methylurapidil (7.27) suggests the non-involvement of an .alpha.1A-or
an .alpha.1D-adrenoceptor; the low pA2 value for HV723 (8.47) was similar

L14 ANSWER 98 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
to that against responses postulated as .alpha.1L. The authors conclude
that rabbit cutaneous resistance arteries express a prazosin-sensitive
functional .alpha.1-adrenoceptor resembling the .alpha.1B and another low
affinity site for prazosin which on the basis of the functional antagonism
produced by HV723 most closely resembles the .alpha.1L-adrenoceptor; the
low pA2 value for HV723 (8.47) is similar to that against responses
postulated as .alpha.1L.
IT **21102-95-4**, BMY7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.alpha.1-adrenoceptor subtypes mediating vasoconstriction in rabbit
cutaneous resistance arteries)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



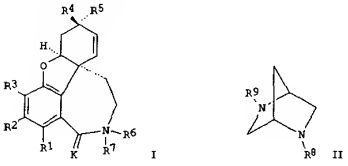
●2 HCl

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:717921 CAPLUS
DOCUMENT NUMBER: 128:13368
TITLE: New benzazepine derivatives, medicaments containing
the same and their use to prepare medicaments
INVENTOR(S): Czollner, Laszlo; Frohlich, Johannes; Jordis, Ulrich;
Kuenburg, Bernhard
PATENT ASSIGNEE(S): Sanochemia Ltd., Malta; Czollner, Laszlo; Frohlich,
Johannes; Jordis, Ulrich; Kuenburg, Bernhard
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9740049	A1	19971030	WO 1997-AT74	19970421
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AT 9600716	A	19971015	AT 1996-716	19960419
AT 403803	B	19980525		
AU 9724985	A1	19971112	AU 1997-24985	19970421
EP 897387	A1	19990224	EP 1997-916263	19970421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, FI				
NO 9804852	A	19981116	NO 1998-4852	19981016

PRIORITY APPLN. INFO.: AT 1996-716 19960419
WO 1997-AT74 19970421
OTHER SOURCE(S): MARPAT 128:13368
GI

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

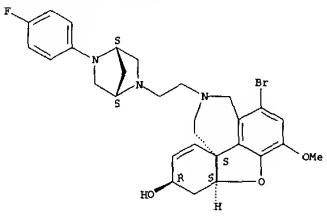


I

II

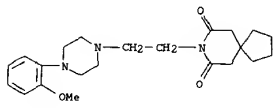
AB The synthesis of benzofuro[3a,3,2,ef][2]benzazepines (I) [R1,R2 = H, halo,
CN, NC, OH, SH, SO3H, NH2, CF3, (un)substituted alkyl, (un)substituted
alkoxy, (un)substituted aryl, (un)substituted aryloxy; R3 = OH, OMe; R4,R5
= H2, O, substituted O, (un)substituted alkyl, (un)substituted aryl,
(un)substituted alkenyl, (un)substituted alkynyl, (un)substituted
hydrazone, (un)substituted oxime; X = H2, O] and diazabicyclo[2.2.1]heptanes (II) [R8 = CH2Ph, 4-MeC6H4SO2, H, (un)substituted alkyl, Me3CO2C; R9 = (un)substituted Ph, CH2Ph, CHPh2,
Me3CO2C] are described. Thus, I (R1 = Br, R2 = H, R3 = OMe, R4 = OH, R5 =
H, R6 = H, X = H2) (III) was prepd. by tartrate resoln. of (.+-.)-N-demethyl-8-bromogalanthamine. III in in vitro study showed an
IC50 of >150 in .upsilon.mol for the inhibition of acetylcholine esterase.
Also disclosed are medicaments which contain compds. of formulas (I) and/or (II) and may be successfully used for treating Alzheimer disease
and related demential states, as well as the Langdon-Down syndrome.
IT **198988-64-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzazepine galanthamine analogs and diazabicycloheptanes
for use in treatment of dementia)
RN 198988-64-6 CAPLUS
CN 6H-Benzofuro[3a,3,2-ef][2]benzazepin-6-ol, 1-bromo-11-[2-[5-(4-fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]ethyl]-4a,5,9,10,11,12-hexahydro-3-methoxy-, [4a.alpha.,6.beta.,8aR*,11(1R*,4R*)]- (9CI) (CA
INDEX NAME)

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
Relative stereochemistry.



L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:713805 CAPLUS
DOCUMENT NUMBER: 128:18928
TITLE: Antagonism to noradrenaline-induced lethality in rats is related to affinity for the .alpha.1A-adrenoceptor subtype
AUTHOR(S): Testa, Rodolfo; Guarneri, Luciano; Ibba, Marina; Angelico, Patrizia; Poggesi, Elena; Taddei, Carlo; Motta, Gianni; Leonardi, Amedeo
CORPORATE SOURCE: Pharmaceutical RandD Division, RECORDATI S.p.A., Milan, 20148, Italy
SOURCE: Life Sciences (1997), 61(22), 2177-2188
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potency of several .alpha.1-adrenoceptor antagonists in preventing the noradrenaline-induced lethality in conscious rats, their binding affinity for the native .alpha.1A- and .alpha.1B-adrenoceptors, the recombinant animal .alpha.1a-, .alpha.1b- and .alpha.1d-adrenoceptor subtypes, as well as their functional affinity for the .alpha.1L-adrenoceptor subtype were evaluated. The potency of the tested compds. as antagonists of noradrenaline-induced lethality was correlated with the affinity for the .alpha.1A- (and .alpha.1a-) adrenoceptor subtype, but not with the affinity for the other subtypes. On the contrary, the hypotensive effects of the compds., assessed in anesthetized rats, were not clearly related with the affinity for any of the .alpha.1-subtypes. These results suggest that the .alpha.1A-subtype plays a detg. role in preventing lethality induced by noradrenaline in the rats, and that this activity is unrelated to the hypotensive effect of the compds., which cannot be clearly correlated with affinity for a particular .alpha.1-adrenoceptor subtype.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonism to noradrenaline-induced lethality relation to affinity for .alpha.1A-adrenoceptor subtype)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

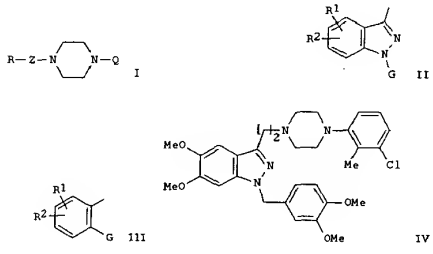


●2 HCl

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:701490 CAPLUS
DOCUMENT NUMBER: 128:22921
TITLE: Preparation of piperazines having calmodulin inhibitory activity
INVENTOR(S): Yamamoto, Kenjiro; Hasegawa, Atsushi; Kubota, Hideki; Andodeceased, Masahiro; Yamaguchi, Hitoshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 242,842, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

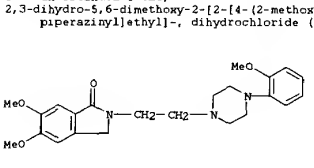
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5681954	A	19971028	US 1995-416311	19950404
PRIORITY APPLN. INFO.:			JP 1993-11277	19930514
			US 1994-242842	19940516

OTHER SOURCE(S): MARPAT 128:22921
GI

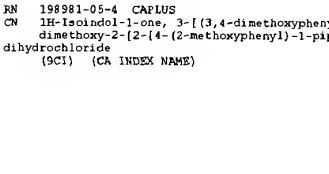


AB The title compds. [I; Q = C1-6 alkyl, C1-6 alkoxy, CF3, etc.; R = II or III (wherein G = C1-6 alkyl, (un)substituted Ph, etc.; R1, R2 = C1-6 alkyl, C1-6 alkoxy, CF3, etc.); Z = C1-3 alkylene, C2-4 alkenylene, C(O), etc.], useful as a treating agent for diseases in the circulatory organs

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
or in the cerebral region which are caused by excessive activation of calmodulin, were prepd. Thus, treatment of 1-{[5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl]acetyl}-4-(3-chloro-2-methylphenyl)piperazine with BH3*THF in THF afforded the title compd. IV which showed 19.2% increase of survival time on nitrogen-induced hypoxia model in mouse, and IC50 of 3.1 against calmodulin-dependent PDE.
IT **198980-97-1P 198981-00-9P 198981-05-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazines having calmodulin inhibitory activity)
RN 198980-97-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



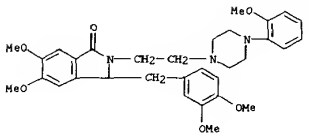
RN 198981-00-9 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 198981-05-4 CAPLUS
CN 1H-Isoindol-1-one, 3-[(3,4-dimethoxyphenyl)methyl]-2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



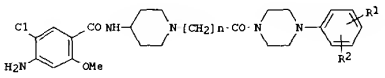
●2 HCl

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:618726 CAPLUS
DOCUMENT NUMBER: 127:293254
TITLE: Preparation of N-(1-substituted-4-piperidyl)benzamides having serotonin receptor agonist activity
INVENTOR(S): Yuasa, Teruyuki; Tanaka, Yuji; Khlebnikov, Vladimir
Alesevich; Shimamura, Masahiro; Ikeda, Akira; Kobayashi, Hideyuki; Chaki, Etsuko; Takahashi, Kazuyoshi
PATENT ASSIGNEE(S): Morishita Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09241241	A2	19970916	JP 1996-80693	19960308

OTHER SOURCE(S): MARPAT 127:293254
GI



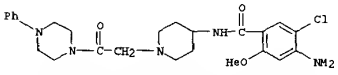
I

AB Title compds. I (R1, R2 = H, halo, lower alkoxy, lower alkyl; X = CO, methylene; n = 1-3) and their pharmaceutically acceptable salts are prepd. 4-Amino-5-chloro-2-methoxy-N-(4-piperidyl)benzamide hydrochloride was treated with 1-(3-chloro-1-oxo-1-propyl)-4-(2-methoxyphenyl)piperazine in HCONMe2 in the presence of Na2CO3 and NaI at 80.degree. for 4 h to give 97% I (R1 = 2-MeO, R2 = H, X = CO, n = 2) (II), which was treated with oxalic acid in MeOH to give 1.61 g II oxalate. II oxalate showed EC50 of 20.5 nM for relaxation of carbachol-contracted esophageal smooth muscle of a rat.

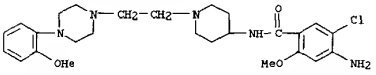
IT **197069-60-6P 197069-63-9P 197069-68-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N-(1-substituted-4-piperidyl)benzamides having serotonin agonist activity)

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

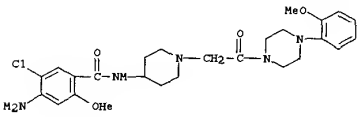
RN 197069-60-6 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 197069-63-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 197069-68-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



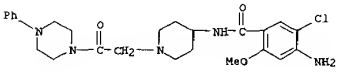
IT **197069-61-7P 197069-64-0P 197069-69-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(1-substituted-4-piperidyl)benzamides having serotonin agonist activity)

RN 197069-61-7 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

CRN 197069-60-6
CMF C25 H32 Cl N5 O3



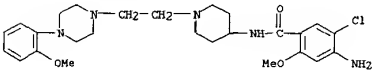
CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 197069-64-0 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 197069-63-9
CMF C26 H36 Cl N5 O3



CM 2

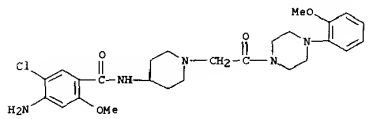
CRN 144-62-7
CMF C2 H2 O4

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 197069-69-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 197069-68-4
CMF C26 H34 Cl N5 O4



CM 2

CRN 144-62-7
CMF C2 H2 O4

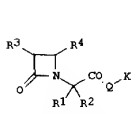
L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:576686 CAPLUS
DOCUMENT NUMBER: 127:234215
TITLE: Preparation of non-peptidyl vasopressin V1a receptor antagonists
INVENTOR(S): Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hunden, David C.; Kaldor, Stephen W.; Koppel, Gary A.; Rizzo, John R.; Skelton, Jeffrey James; et al.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hunden, David C.; Kaldor, Stephen W.; Koppel, Gary A.
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730707	A1	19970828	WO 1997-US3039	19970220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9719779	A1	19970910	AU 1997-19779	19970220
EP 939632	A1	19990908	EP 1997-907895	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2000504731	T2	20000418	JP 1997-529647	19970220
US 6204260	B1	20010320	US 1999-125737	19990819
US 2002049187	A1	20020425	US 2000-733430	20001208

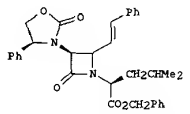
PRIORITY APPLN. INFO.:
US 1996-12149P P 19960223
US 1996-12188P P 19960223
US 1996-12215P P 19960223
GB 1996-5044 A 19960309
GB 1996-5045 A 19960309
GB 1996-5046 A 19960309
WO 1997-US3039 W 19970220
US 1999-125737 A3 19990819

OTHER SOURCE(S): MARPAT 127:234215
GI

L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



I



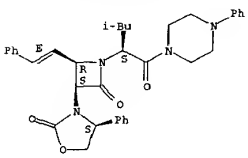
II

AB Azetidinones I [R1 = H, alkyl, carbamoyl, alkoxy, acyl, benzoyl, phenyl; R2 = H, OH, alkyl; R3 = phthalimido, azido, phenoxyacetamido, oxazolinyl, imidazolinyl, pyrrolidinyl, ureido; Q = O, S, NR5; K = H, alkyl; R5 = H, alkyl, OH, alkoxycarbonyl, benzyl] were prepd. for use as vasopressin V1a receptor antagonists. Thus, azetidinone II was prepd. starting from L-leucine benzyl ester, cinnamaldehyde, and 2-[4(S)-phenyloxazolidin-2-on-3-yl]acetyl chloride. II gave an IC50 value of 39 nM when tested for vasopressin V1a receptor binding affinity.

IT **195310-53-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-peptidyl vasopressin V1a receptor antagonists)

RN 195310-53-3 CAPLUS
CN Piperazine, 1-[4-methyl-1-oxo-2-[2-oxo-3-(2-oxo-4-phenyl-3-oxazolidinyl)-4-(2-phenylethenyl)-1-azetidinyl]pentyl]-4-phenyl-, [3S-[1(R*),3.alpha.(R*),4.alpha.(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

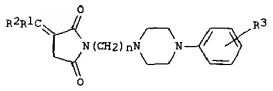


L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:549258 CAPLUS
DOCUMENT NUMBER: 127:149085
TITLE: arylpiperazinylalkylsuccinimides with 5-HT1A and adrenergic.alpha.1 affinity
INVENTOR(S): Lopez Rodriguez, Ma. Luz; Morcillo Ortega, Ma. Jose; K. Rovat, Tandu; Fernandez Velando, Esther; Rosado Samitier, Ma. Luisa; Oresanz Muno, Luis Miguel
PATENT ASSIGNEE(S): Universidad Complutense De Madrid, Spain
SOURCE: Span., 10 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2094690	A1	19970116	ES 1994-2396	19941122
ES 2094690	B1	19970801		

OTHER SOURCE(S): MARPAT 127:149085
GI



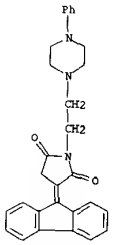
I

AB Title compds. I [R1, R2 = Ph, R1R2 = o-C6H4C6H4-o; R3 = H, alkyl, halogen, olkoxy; n = 1-4] were prepd. Thus, fluorenone was treated with succinonitrile to give 3-(9H-fluoren-9-ylidene)pyrrolidine-2,5-dione which was treated with 1-(3-trifluoromethylphenyl)piperazine to give I [R1R2 = o-C6H4C6H4-o, R3 = 3-CF3, n = 1, II]. II had 5-Ht1A affinity of 44.1 nM and .alpha.1 affinity of >1000 nM.

IT **193287-12-6P 193287-13-7P 193287-14-8P 193287-15-9P 193287-16-0P 193287-17-1P 193287-18-2P 193287-19-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylpiperazinylalkylsuccinimides with 5-HT1A and adrenergic.alpha.1 affinity)

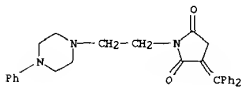
RN 193287-12-6 CAPLUS

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-phenyl-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

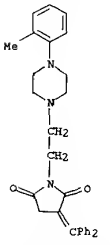
RN 193287-13-7 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

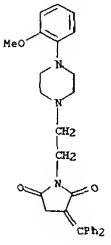
RN 193287-14-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

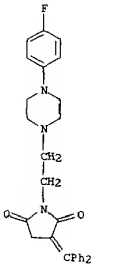
RN 193287-15-9 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

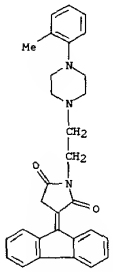
RN 193287-16-0 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

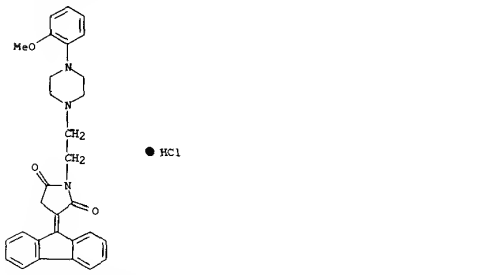
RN 193287-17-1 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 193287-18-2 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-(2-methoxyphenyl)-1-

piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 193287-19-3 CAPLUS
CN 2,5-Pyrrolidinedione,
3-(9H-fluoren-9-ylidene)-1-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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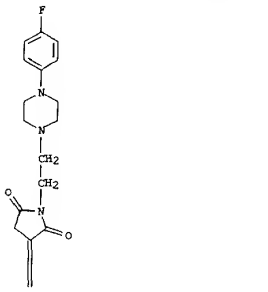
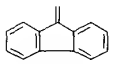


PAGE 2-A



L14 ANSWER 105 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:532196 CAPLUS
DOCUMENT NUMBER: 127:200050
TITLE: Nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compounds, preparation thereof, compositions containing them, and use in treatment of human impotence or erectile dysfunction
INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saenz De Tejada, Inigo
PATENT ASSIGNEE(S): Nitromed, Inc., USA; Garvey, David S.; Schroeder, Joseph D.; Saenz De Tejada, Inigo
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

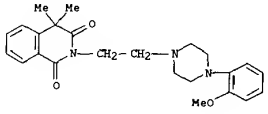
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9727749	A1	19970807	WO 1997-US1294	19970128
W: AU, CA, IL, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9717562	A1	19970822	AU 1997-17562	19970128
AU 721247	B2	20000629		
JP 2000505424	T2	20000509	JP 1997-537755	19970128
EP 1018879	A1	20000719	EP 1997-904887	19970128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6294517	B1	20010925	US 1998-145143	19980901
US 6323211	B1	20011127	US 1999-285048	19990402
US 6417162	B1	20020709	US 1999-306809	19990507
US 6433182	B1	20020813	US 1999-306805	19990507

PRIORITY APPLN. INFO.: US 1996-595732 A 19960202
US 1996-714313 A 19960918
WO 1997-US1294 W 19970128
US 1998-145143 A2 19980901

OTHER SOURCE(S): MARPAT 127:200050

AB Disclosed are nitrosated and nitrosylated .alpha.-adrenergic receptor antagonists; compns. of an .alpha.-adrenergic receptor antagonist optionally substituted with .gtoreq.1 NO or NO2 moiety, and a compd. that donates, transfers, or releases nitric oxide as a charged species, i.e., nitrosonium or nitroxyl, or as the neutral species, nitric oxide; and uses for each of them in treating human impotence or erectile dysfunction. Prepn. of compds. of the invention, e.g. N-(N-L-.gamma.-glutamyl-S-nitroso-L-cysteinyl)glycine and 4-[2-(dimethylamino)ethoxy]-2-methyl-5-(1-methylethyl)phenol-(3-S-nitroso-3-methylbutyric acid)ester. The effect of selected compds. on erectile response in rabbits was detd.

IT **67339-62-2**, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compds., prepn., compns., adrenergic antagonist-NO donor combinations, and use in treatment of human impotence or erectile dysfunction)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:461620 CAPLUS
DOCUMENT NUMBER: 127:81465
TITLE: Preparation of pyrroloazepine derivatives as serotonin-2 receptor antagonists
INVENTOR(S): Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata, Norio
PATENT ASSIGNEE(S): Suntory Limited, Japan; Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata, Norio
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720845	A1	19970612	WO 1996-JP3522	19961202
W: AU, CA, HU, IL, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2212092	AA	19970612	CA 1996-2212092	19961202
AU 9676558	A1	19970627	AU 1996-76558	19961202
AU 719230	B2	20000504		
EP 807632	A1	19971119	EP 1996-939340	19961202
EP 807632	B1	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
IL 121432	A1	20000928	IL 1996-121432	19961202
AT 216388	E	20020515	AT 1996-939340	19961202
US 5962448	A	19991005	US 1997-875495	19970821
US 6258805	B1	20010710	US 1999-312713	19990517
US 2002072515	A1	20020613	US 2001-801816	20010309

PRIORITY APPLN. INFO.: JP 1995-335714 A 19951201
JP 1996-46928 A 19960209
WO 1996-JP3522 W 19961202
US 1997-875495 A2 19970821
US 1999-312713 A1 19990517

OTHER SOURCE(S): MARPAT 127:81465
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; ring P = (un)substituted pyrrole ring; A = alkylene, alkenylene, alkynylene; Y = N-contg. heterocyclyl, etc; Z1, Z2 = H, lower alkyl; dotted line = bond or none] are prepd. I, having a potent serotonin-2 receptor antagonism, are reduced in toxicity and side effects,

L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA INDEX NAME)

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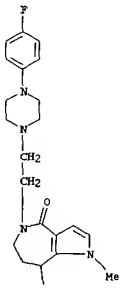
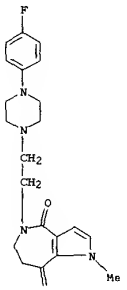


PAGE 2-A

L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and are useful as therapeutic agents for circulatory diseases such as ischemic heart diseases, cerebrovascular disorders, and peripheral circulatory disturbances. Thus, pyrroloazepine deriv. (II) (prepn. given) was reacted with HSCH2CH2SH in the presence of BF3.Et2O in AcOH to give 79% the title compd. (III), which at 10-8 M showed 75.5% inhibitory activity against serotonin (5-HT).
IT **191591-85-2P 191592-08-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrroloazepine derivs. as serotonin-2 receptor antagonists)
RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)

PAGE 1-A

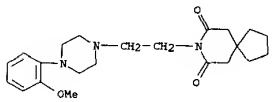


PAGE 2-A

RN 191592-08-2 CAPLUS

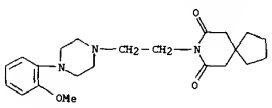
L14 ANSWER 107 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:430404 CAPLUS
DOCUMENT NUMBER: 127:134218
TITLE: In vivo electrophysiological characterization of 5-HT receptors in the guinea pig head of caudate nucleus and orbitofrontal cortex
AUTHOR(S): Mansari, M. El; Blier, P.
CORPORATE SOURCE: Neurobiological Psychiatry Unit, McGill Univ., Montreal, QC, H3A 1A1, Can.
SOURCE: Neuropharmacology (1997), 36(4/5), 577-588
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present study was to characterize in vivo the 5-HT receptor subtypes which mediate the effect of microiontophoretic applied 5-HT in the guinea pig head of caudate nucleus and orbitofrontal cortex. 5-HT and the preferential 5-HT2A receptor agonist DOI and the preferential 5-HT2C receptor agonist mCPP, suppressed the quisqualate (QUIS)-induced activation of neurons in both structures. The inhibitory effect of DOI and mCPP was not prevented by acute i.v. administration of the 5-HT1/2 receptor antagonist metergoline (2 mg/kg) and the 5-HT2A/2C receptor antagonist ritanserin (2 mg/kg) in the two regions nor by the selective 5-HT2A receptor antagonist MDL100907 (1 mg/kg) in the head of caudate nucleus. However, the inhibitory effect of DOI, but not that of mCPP, was antagonized by a 4-day treatment with metergoline and ritanserin (2 mg/kg/day; using minipumps implaced s.c.) in the head of caudate nucleus, but not in the orbitofrontal cortex. Microiontophoretic ejection of the 5-HT1A/7 receptor agonist 8-OH-DPAT and of the 5-HT1A receptor antagonist WAY100635 both suppressed the spontaneous and QUIS-activated firing activity of the orbitofrontal cortex neurons. At currents which did not affect the basal discharge activity of the neuron recorded, microiontophoretic application of WAY100635 and BMY7378 failed to prevent the inhibitory effect of 8-OH-DPAT. The inhibitory effect of gepirone, which is a 5-HT1A receptor agonist but devoid of affinity for 5-HT7 receptors, was also not antagonized by WAY100635. Altogether, these results suggest the presence of atypical 5-HT1A receptors in the orbitofrontal cortex. The present results also indicate that the suppressant effect of DOI may be mediated by 5-HT2A receptors in the head of caudate nucleus and atypical 5-HT2 receptors in the orbitofunctional

L14 ANSWER 107 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
cortex.
IT **21102-95-4**, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(characterization of 5-HT receptors in guinea pig head of caudate nucleus and orbitofrontal cortex in relation to obsessive compulsive
disorder)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 108 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

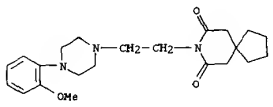


●2 HCl

L14 ANSWER 108 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:406096 CAPLUS
DOCUMENT NUMBER: 127:130790
TITLE: .alpha.1-Adrenoceptor subtype selectivity: molecular
modeling and theoretical quantitative structure-affinity relationships
AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.; Testa, R.; Leonardi, A.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena,
41100, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(5), 809-816
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study constitutes a preliminary rationalization, at the mol. level,
of antagonist selectivity towards the three cloned .alpha.1-adrenergic receptor (.alpha.1-AR) subtypes. Mol. dynamics simulations allowed a structural/dynamics anal. of the seven .alpha.-helix-bundle models of the
bovine .alpha.1a-, hamster .alpha.1b-, and rat .alpha.1d-AR subtypes. The
results showed that the transmembrane domains of these subtypes have different dynamic behaviors and different topogs. of the binding sites,
which are mainly constituted by conserved residues. In particular, the
.alpha.1a-AR binding site is more flexible and topog. different with respect to the other two subtypes. The results of the theor. structural/dynamics anal. of the isolated receptors are consistent with
the binding affinities of the 16 antagonists tested towards the three cloned .alpha.1-AR subtypes. Moreover, the theor. quant. structure-affinity relationships obtained from the antagonist-receptor interaction models further corroborate the hypothesis that selectivity towards one preferential subtype is mainly modulated by receptor and/or
ligand distortion energies. In other words, subtype selectivity seems to
be mainly guided by the dynamic complementarity (induced fit) between ligand and receptor. On the basis of the quant. models presented it is
possible to predict both affinities and selectivities of putative .alpha.1-AR ligands as well as to est. the theor. .alpha.1-AR subtype affinities and selectivities of existing antagonists.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); BIOL (Biological study)
(mol. modeling and QSAR of .alpha.1-Adrenoceptor subtype selectivity)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 109 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:331431 CAPLUS
DOCUMENT NUMBER: 127:60478
TITLE: Analysis of .alpha.1-adrenoceptors in rabbit lower urinary tract and mesenteric artery
AUTHOR(S): Van der Graaf, Pieter H.; Deplanne, Valerie; Duquenne,
Chantal; Angel, Itzchak
CORPORATE SOURCE: Synthelabo Recherche (L.E.R.S.), Department of Internal Medicine, B.P. 248, 10 rue des Carrieres, Rueil Malmaison, 92500, Fr.
SOURCE: European Journal of Pharmacology (1997), 327(1), 25-32
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, we have investigated the effects of a series of .alpha.1-adrenoceptor antagonists on the phenylephrine-mediated
contractions of rabbit isolated prostate, urethra, trigone and mesenteric
artery. With the exception of RS-17053 (N-[2-(2-cyclopropylmethoxyphenoxy)ethyl]-5-chloro-.alpha.,.alpha.-dimethyl-1H-indole-3-ethanamine hydrochloride), the antagonists displayed the lowest
potency in the urethra. Catecholamine uptake1 and uptake2 appeared not to
be the cause for the low pKB /pA2 values obtained in the urethra because
cocaine and corticosterone had no effect on the potency of phenylephrine
in this tissue. The low potencies displayed by prazosin, RS-17053 and HV723 (.alpha.-ethyl-3,4,5-trimethoxy-.alpha.-(3-((2-(2-methoxyphenoxy)ethyl)amino)propyl)benzene-acetonitrile fumarate) suggest
that the functional receptors in all four tissues belong to the .alpha.1L-adrenoceptor class. Whether or not the significant between-tissue differences in antagonist potencies are due to heterogeneity of this receptor class remains to be elucidated.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(pharmacol. characteristics of the .alpha.1-adrenoceptors in rabbit lower urinary tract and mesenteric artery)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 109 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:234024 CAPLUS
DOCUMENT NUMBER: 127:1136
TITLE: Is .alpha.1D-adrenoceptor protein detectable in rat
tissues?
AUTHOR(S): Yang, Ming; Verfurth, Frank; Buscher, Rainer; Michel,
Martin C.
CORPORATE SOURCE: Department Medicine, University Essen, Essen, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1997),
355(4), 438-446
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

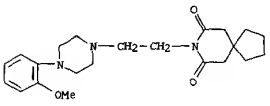
AB We have used the .alpha.1D-adrenoceptor selective antagonist, BMY 7378,
the .alpha.1D-selective agonists, adrenaline and phenylephrine, the .alpha.1A-selective antagonists, (+)-niguldipine, SB 216469 and WB4101,
and the non-subtype-selective .alpha.1-adrenoceptor antagonist, nemonapride, to investigate the presence of .alpha.1D-adrenoceptors in rat
tissues at the protein level. Radio-ligand binding studies using [3H]prazosin as the radio-ligand were performed in three tissues contg.
.alpha.1D- adrenoceptor mRNA, spleen, cerebral cortex and kidney, and in
comparison in one tissue not contg. .alpha.1D-adrenoceptor mRNA, liver.
Cerebral cortex and kidney were also studied upon .alpha.1B-adrenoceptor
inactivation by chloroethylclonidine treatment (10 .mu.M, 30 min, 37.degree.). Expts. with cloned rat .alpha.1-adrenoceptor subtypes
transiently expressed in COS cells confirmed the known selectivity of the
investigated drugs for .alpha.1-adrenoceptor subtypes or the lack thereof
of nemonapride. Accordingly nemonapride had steep and monophasic
competition curves in all native and chloroethylclonidine-treated tissues.
BMY 7378 also had steep and monophasic competition curves and low affinity
in all native tissues. In contrast, adrenaline and phenylephrine (in the
presence of 100 .mu.M GTP) had monophasic competition curves of low
affinity in liver and spleen but biphasic competition curves in cerebral
cortex and kidney. Following chloro-ethylclonidine treatment competition
curves for adrenaline, phenylephrine, (+)-niguldipine, SB 216469 and WB
4101 remained biphasic in cerebral cortex and kidney while those for
nemonapride remained monophasic. We conclude that .alpha.1D-adrenoceptors

L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

are not readily detectable at the protein level in a variety of rat
tissues where their mRNA is expressed. The biphasic competition curves of
some agonists and antagonists in chloroethyl-clonidine-treated rat tissues
do not represent .alpha.1D-adrenoceptors and are not readily explained by
the present .alpha.1A/.alpha.1B/.alpha.1D-adrenoceptor classification.

IT **21102-95-4**, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(investigations of presence of .alpha.1D-adrenoceptors in rat tissues
at protein level)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS

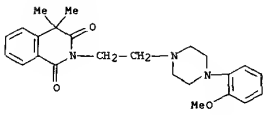
ACCESSION NUMBER: 1997:220142 CAPLUS
DOCUMENT NUMBER: 127:76453
TITLE: .alpha.2C-adrenoceptors mediate contractile responses
to noradrenaline in the human saphenous vein
AUTHOR(S): Gavin, K. T.; Colgan, M. P.; Moore, D.; Shanik, G.;
Docherty, J. R.
CORPORATE SOURCE: Department Physiology, Royal College Surgeons, Dublin,
Ire.
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1997),
355(3), 406-411
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Postjunctional .alpha.2-adrenoceptors in the saphenous vein were
investigated for the ability of .alpha.2-adrenoceptor antagonists to shift
the contractile potency of noradrenaline. The following antagonists were
employed : chlorpromazine, BDF 8933, prazosin, ARC 239, yohimbine, HV 723,
WB 4101, SKF 104078, and BRL 44408. Antagonist potency at postjunctional
.alpha.2-adrenoceptors was correlated with antagonist affinity at
.alpha.2-adrenoceptor ligand binding sites in membranes of human platelet
(.alpha.2), rat kidney (.alpha.2B) and Sf 9 cells expressing human
recombinant. receptors (.alpha.2C). The correlation with the
postjunctional .alpha.2-adrenoceptor mediating contraction of the
saphenous vein was best for the human recombinant .alpha.2C-adrenoceptor
ligand binding site, as compared to correlations with the
.alpha.2B-adrenoceptor ligand binding site of rat kidney and with the
.alpha.2A-adrenoceptor ligand binding site of human platelet. It is
concluded that the functional postjunctional a2-adrenoceptor mediating
contractions of the saphenous vein closely resembles the human recombinant
a2C-adrenoceptor ligand binding site.

IT **67339-62-2**, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(affinity of, at the .alpha.2-adrenoceptor ligand binding sites in human platelet, rat kidney, human recombinant receptors and potencies
in saphenous vein)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 112 OF 263 CAPLUS COPYRIGHT 2002 ACS

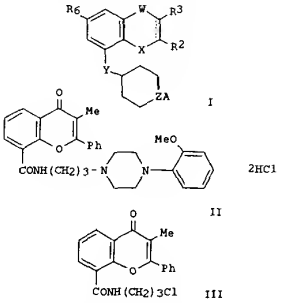
ACCESSION NUMBER: 1997:169157 CAPLUS
DOCUMENT NUMBER: 126:225315
TITLE: Bicyclic heterocyclic derivatives having .alpha.1-adrenergic and 5HT1A serotonergic activities
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo
PATENT ASSIGNEE(S): Recordati S.A., Chemical and Pharmaceutical Company, Switz.
SOURCE: U.S., 84 pp., Cont.-in-part of U.S. 5,474,994. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5605896	A	19970225	US 1994-299188	19940831
US 5403842	A	19950404	US 1992-888775	19920526
AU 9336296	A1	19930913	AU 1993-36296	19930223
RO 112111	B3	19970530	RO 1994-1404	19930223
PL 175556	B1	19990129	PL 1993-304889	19930223
RU 2128656	C1	19990410	RU 1994-43324	19930223
SK 280143	B6	19990910	SK 1994-1007	19930223
ZA 9301278	A	19931118	ZA 1993-1278	19930224
LT 3038	B	19940925	LT 1993-354	19930224
CN 1079738	A	19931222	CN 1993-105852	19930526
CN 1040434	B	19981028		
US 5474994	A	19951212	US 1993-67861	19930526
FI 9403876	A	19940823	FI 1994-3876	19940823
NO 9403140	A	19940825	NO 1994-3140	19940825

PRIORITY APPLN. INFO.: IT 1992-MI408 A 19920225
US 1992-888775 A2 19920526
US 1993-67861 A2 19930526
EP 1993-301264 A 19930222
WO 1993-EP420 A 19930223

OTHER SOURCE(S): MARPAT 126:225315
GI

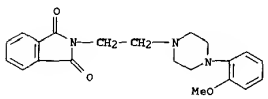
L14 ANSWER 112 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Bicyclic heterocyclic derivs., such as I [X = N, O, S; W = C(O), C(S), CH(OH), bond; R2 = H, optionally substituted alkyl, alkenyl, alkylnyl, carbocycle, heterocycle; R3 = alkyl, hydroxyalkyl, Ph, OH, alkoxy, alkoxyalkyl; R6 = H, halogen, NO2, NH2, AcNH, mono-, dialkylamino, CN, OH, alkoxy, alkyl; Y = CO, CO2, CONH, CH(OH), CH:CH, CH:CHCO2, CH:CHCONH, CH2NH, CH2NHCO, CH2NHSO2, CH2O, CH2S, NH, NHCO, NHCONH, NHSO2, O, S, SO2NH, CONHO, CSNH, NHCO2, COS, CONH(CH2)m, m = 1-6; Z = N, A = (un)substituted Ph, pyrimidinyl, 1,4-benzodioxan-8-yl, benzopyran-8-yl, benzofuran-7-yl, dihydrobenzopyran-8-yl; Z = CH2N; Z = CH, A = one or two Ph, 4-FC6H4CO, 2-oxo-1-benzimidazolinyl, (CH2)nOA, n = 0-2], and their pharmaceutically acceptable salts useful as .alpha.1-adrenergic and 5HT1A serotonergic agents for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders are described. Thus, benzopyran II was prepd. by heating 1-(2-methoxyphenyl)piperazine with benzopyran III at 180.degree. for 5 h. II had IC50 = 29 nM for .alpha.1-adrenergic receptor binding, IC50 = 9 nM for 5HT1A receptor binding, ED25 = 45 .mu.g/kg i.v. hypotensive effect and ED25 = 1.4 .mu.g/kg in Na-induced urethral contractility assays.

IT **99718-67-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bicyclic heterocyclic derivs. having .alpha.1-adrenergic and 5HT1A serotonergic activities)

RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



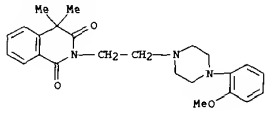
L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:88411 CAPLUS
DOCUMENT NUMBER: 126:259093
TITLE: [3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites. Studies in rabbit kidney membranes
AUTHOR(S): Hosseini, A. R.; King, P. R.; Louis, W. J.; Gundlach, A. L.
CORPORATE SOURCE: Austin Repatriation Med. Cent., University Melbourne, Austin, Australia
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1997), 355(1), 131-138
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2-(2-Benzofuranyl)-2-imidazoline (2-BFI) has recently been characterized as a selective ligand for the I2-type of imidazoline-receptor binding site(s) (I2-RBS). The present studies detd. the relative levels of specific [3H]2-BFI binding to membrane homogenates of brain and kidney from rat, guinea pig and rabbit and identified the pharmacol. characteristics of [3H]2-BFI binding sites in rabbit kidney membranes. Rabbit kidney membranes had the highest relative d. of specific [3H]2-BFI binding of all tissues studied (2000 fmol/mg protein). Rabbit brain and guinea pig kidney had moderate levels of specific [3H]2-BFI binding (350500 fmol/mg protein), while rat kidney and guinea pig and rat brain displayed much lower densities of binding (4065 fmol/mg protein). Studies of [3H]2-BFI binding kinetics in rabbit kidney homogenates revealed binding to two distinct sites with Kd values of 0.10 nmol/l and 1.00 nmol/l resp. Drug inhibition studies revealed that L-adrenaline; .alpha.1-adrenoceptor drugs (prazosin, L-phenylephrine) and .alpha.2-adrenoceptor drugs (rauwolscine, methoxyidazoxan, ARC-239) had extremely low affinities for [3H]2-BFI binding sites (IC50 .gtoreq. 10 .mu.mol/l). Putative I1-RBS compds., p-aminoclonidine, moxonidine, imidazole-4-acetic acid and cimetidine, inhibited [3H]2-BFI binding to rabbit renal membranes with low to very low affinities (Ki values 3 to .gtoreq. 100 .mu.mol/l), suggesting [3H]2-BFI does not label I1-RBS in rabbit kidney membranes. I2-RBS compds.BU224, BU239, idazoxan, and cirazoline inhibited [3H]2-BFI binding confirming the labeling of I2-RBS. Inhibition of [3H]2-BFI binding by certain compds. was consistent with

L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

their interaction with two binding site populations for example (drug, Ki values) guanabenz, 0.65 nmol/l and 0.17 .mu.mol/l; naphazoline, 0.94 nmol/l and 2.8 .mu.mol/l; amiloride, 76 nmol/l and 26 .mu.mol/l rilmenidine, 150 nmol/l and 50 .mu.mol/l; and clonidine, 230 nmol/l and 70 pmol/l. These results demonstrate that [3H]2-BFI is a highly selective and high affinity radioligand for I2-RBS which should be useful for the further characterization of these sites in mammalian tissues.

IT **67339-62-2**, ARC-239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
([3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites in rabbit kidney and brain)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



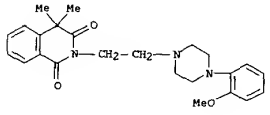
L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:70999 CAPLUS
DOCUMENT NUMBER: 126:113098
TITLE: Investigation of the subtype of .alpha.2-adrenoceptor mediating pressor responses in the pithed rat
AUTHOR(S): Gavin, Katherine; Docherty, James R.
CORPORATE SOURCE: Dep. Physiol., Royal Coll. Surgeons Ireland, Dublin, Ire.
SOURCE: European Journal of Pharmacology (1996), 318(1), 81-87
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have investigated the subtype of .alpha.2-adrenoceptor mediating postjunctional pressor responses in the pithed rat in comparison with .alpha.2-adrenoceptor ligand binding sites. In pithed rats, postjunctional .alpha.2-adrenoceptors were investigated in terms of the ability of .alpha.2-adrenoceptor antagonists to shift the pressor potency of the .alpha.2-adrenoceptor agonist xylazine. Antagonist potency at postjunctional .alpha.2-adrenoceptors in the pithed rat was correlated with antagonist affinity at .alpha.2-adrenoceptor ligand binding sites in membranes of rat kidney (.alpha.2B), Sf9 cells expressing human recombinant receptors (.alpha.2C) and rat submandibular gland (.alpha.2D) labeled with [3H]yohimbine. The correlation with the postjunctional .alpha.2-adrenoceptor mediating pressor responses in the pithed rat was better for the .alpha.2D-adrenoceptor ligand binding site of rat submandibular gland (r = 0.95) and the .alpha.2B-adrenoceptor ligand binding site of rat kidney (r = 0.90) than with the human recombinant .alpha.2C-adrenoceptor ligand binding site (r = 0.81). When the pressor potencies of three addnl. antagonists were included in the correlations for .alpha.2B- and .alpha.2D-sites only, the correlation with .alpha.2D-adrenoceptor ligand binding site of rat submandibular gland (r = 0.91) was much better than with the .alpha.2B-adrenoceptor ligand binding site of rat kidney (r = 0.77). It is concluded that the functional postjunctional .alpha.2-adrenoceptors mediating pressor responses in the pithed rat most closely resemble the .alpha.2D-adrenoceptors subtype.

IT **67339-62-2**, ARC 239
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(subtype of .alpha.2-adrenoceptor mediating pressor responses in pithed

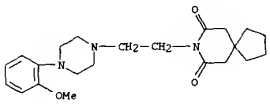
L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

rat in comparison with ligand binding sites)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



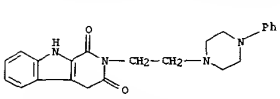
L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:743484 CAPLUS
DOCUMENT NUMBER: 126:152648
TITLE: Reduction of guinea pig pup isolation calls by anxiolytic and antidepressant drugs
AUTHOR(S): Molewijk, H. E.; Hartog, K.; Van Der Poel, A. M.; Mos, J.; Olivier, B.
CORPORATE SOURCE: CNS Pharmacology, Solvay Duphar B. V., Weesp, 1380 DA, Neth.
SOURCE: Psychopharmacology (Berlin) (1996), 128(1), 31-38
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Guinea pigs possess central 5-HT1D receptors similar to humans but different from rats and mice. The effects of a variety of psychotropic drugs on guinea pig pup isolation calls was assessed. Anxiolytic compds. such as the benzodiazepine receptor agonists diazepam and alprazolam, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, and alc. reduced isolation calling by the guinea pig pup. Moreover, mixed antidepressant/anxiolytic compds. like the 5-HT uptake inhibitors fluvoxamine and clomipramine or the MAO-inhibitor clorgyline as well as the antidepressant NA uptake inhibitors desipramine and maprotiline suppressed vocalizations. The 5-HT1D/1A receptor agonist 5-CT was also very effective in reducing sepn. calls. Remarkably, the partial 5-HT1A receptor agonists buspirone and BMY 7378 did not affect calling. The neuroleptic haloperidol, the psychostimulant d-amphetamine, the putative anxiogenics DMCM and m-CPP and the putative anxiolytics ondansetron and CI-988 had no effect on isolation calls of guinea pig pups. This paradigm could be helpful to assess behavioral effects of anxiolytic and antidepressant drugs in a species different from rat or mouse, and in which the effects of 5-HT1D receptor ligands may possibly be established.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(redn. of guinea pig pup isolation calls by anxiolytic and antidepressant drugs)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

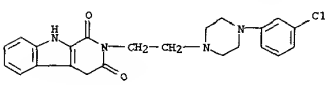


●2 HCl

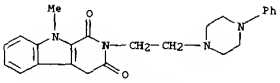
L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:731716 CAPLUS
DOCUMENT NUMBER: 126:31297
TITLE: 4-Aryl-1-piperazinylalkyl derivatives of 1,2,3,4-tetrahydro-.beta.-carboline ring system. Synthesis and preliminary in vivo studies
AUTHOR(S): Cegla, Marek T.; Boksa, J.; Chojnacka-Wojcik, E.; Misztal, S.
CORPORATE SOURCE: Collegium Medicum, Jagiellonian University, Krakow, 30688, Pol.
SOURCE: Pharmazie (1996), 51(12), 932-936
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three series of compds. contg. a 4-aryl-1-piperazinylalkyl fragment attached to different positions of indole or 1,2,3,4-tetrahydro-.beta.-carboline were prepd. A quant. relationship between the structure of some derivs. and their sedative effect was found using the Free-Wilson approach.
IT **184691-40-5P 184691-41-6P 184691-43-8P 184691-44-9P 184691-51-8P 184691-52-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., sedative effect, antiserotonin activity, and QSAR of (arylpiperazinylalkyl)tetrahydrocarbolines)
RN 184691-40-5 CAPLUS
CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 4,9-dihydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



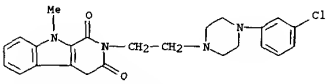
RN 184691-41-6 CAPLUS
CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,9-dihydro- (9CI) (CA INDEX NAME)



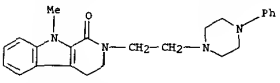
L14 RNSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 184691-43-8 CAPLUS
CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 4,9-dihydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



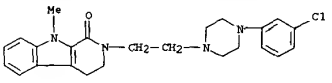
RN 184691-44-9 CAPLUS
CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,9-dihydro-9-methyl- (9CI) (CA INDEX NAME)



RN 184691-51-8 CAPLUS
CN 1H-Pyrido[3,4-b]indol-1-one, 2,3,4,9-tetrahydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 184691-52-9 CAPLUS
CN 1H-Pyrido[3,4-b]indol-1-one, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3,4,9-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)



L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 117 OF 263 CAPLUS COPYRIGHT 2002 ACS

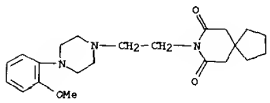
ACCESSION NUMBER: 1996:673359 CAPLUS
DOCUMENT NUMBER: 125:318433
TITLE: Pharmacological evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery
AUTHOR(S): Delaflotte, S.; Auguet, M.; Chabrier, P. E.
CORPORATE SOURCE: Institut Henri Beaufour Research Labs., Les Ulis, Fr.
SOURCE: Acta Physiologica Scandinavica (1996), 158(3), 241-251
CODEN: APSCAX; ISSN: 0001-6772
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The .alpha.1-adrenoceptor subtypes mediating contraction of rabbit prostate and hypogastric artery were pharmacol. characterized using an isolated organ bath technique. The prostate had the same sensitivity to the contractile action of methoxamine and phenylephrine, whereas the hypogastric artery was five times less sensitive to the action of methoxamine in comparison with phenylephrine. Clonidine elicited contraction in the hypogastric artery but not in the prostate. BMY7378 was about 70-fold more potent to antagonize the phenylephrine-induced contraction in the hypogastric artery (pA2, 8.14) than in the prostate (pA2 6.28), and 5-methyl-urapidil was about three-fold more potent on prostrate than on hypogastric artery. The potency of different .alpha.1 -adrenoceptor antagonists tested in the rabbit prostate was significantly correlated with their binding affinity for the expressed recombinant .alpha.1A-, but no .alpha.1B - or .alpha.1D-, adrenoceptor subtype, whereas, the potency of the .alpha.1-adrenoceptor antagonists tested in the rabbit hypogastric artery was better correlated with the defined .alpha.1D -adrenoceptor. Chloroethylclonidine produced a 10-fold rightward shift in the phenylephrine concn.-response curve in the hypogastric artery but only had a weak effect in the prostate. The results indicates that significant heterogeneity exists among .alpha.1 -adrenoceptor in the rabbit hypogastric artery (.alpha.1D-adrenoceptor) and the prostate (.alpha.1A-adrenoceptor).

IT **21102-95-4**, BMY7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pharmacol. evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 117 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 118 OF 263 CAPLUS COPYRIGHT 2002 ACS

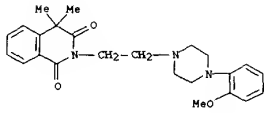
ACCESSION NUMBER: 1996:595110 CAPLUS
DOCUMENT NUMBER: 125:318251
TITLE: The subtype-selective .alpha.2-adrenoceptor antagonists BRL 44408 and ARC 239 also recognize 5-HT1A receptors in the rat brain
AUTHOR(S): Meana, J. Javier; Callado, Luis F.; Pazos, Angel; Grijalba, Bernardo; Garcia-Sevilla, Jesus A.
CORPORATE SOURCE: Department of Pharmacology, University of the Basque Country, E-48940, Leioa, Spain
SOURCE: European Journal of Pharmacology (1996), 312(3), 385-388
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several .alpha.2-adrenoceptor compds. have been reported to recognize 5-HT1A receptors. The interaction of the .alpha.2A/D- and .alpha.2B/C-adrenoceptor antagonists BRL 44408 (2-[2H-(1-methyl-1,3-dihydroisoindole) methyl]-4,5-dihydroimidazole) and ARC 239 (2-[2-[4-(o-methoxyphenyl)piperazin-1-yl] ethyl]-4,4-dimethyl-1,3-(2H,4H)-isoquinolinedione) with 5-HT1A receptors was evaluated in rat brain. Competition expts. in cortex with both compds. against the specific binding of the 5-HT1A receptor radioligand [3H]8-OH-DPAT (8-hydroxy-2-(n-dipropyl-amine)-tetralin) yielded Ki values in the nanomolar range, fairly close to their previously reported affinities for .alpha.2-adrenoceptors. Similar Ki values were obtained under .alpha.2-adrenoceptor masking conditions by competition assays of these compds. against the .alpha.2-adrenoceptor and 5-HT1A receptor radioligand [3H]RX 821002 (2-methoxy idazoxan) specific binding in hippocampus. The results indicate that BRL 44408 and ARC 239 recognize 5-HT1A receptors in addn. to .alpha.2-adrenoceptors. The fact should be considered when using these compds. to study .alpha.2-adrenoceptor subtypes.

IT **67339-62-2**, Arc239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(subtype-selective .alpha.2-adrenoceptor antagonists BRL 44408 and ARC 239 recognize 5-HT1A receptors in rat brain)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 118 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

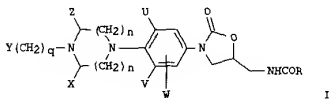


L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:537790 CAPLUS
DOCUMENT NUMBER: 125:221870
TITLE: (Piperazinylphenyl)oxazolidinone antimicrobials
INVENTOR(S): Hutchinson, Douglas K.; Barbachyn, Michael R.; Brickner, Steven J.; Gammill, Ronald B.; Patel, Mahesh V.
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 880,432, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5547950	A	19960820	US 1994-332822	19941031
HU 72296	A2	19960429	HU 1994-3208	19930421
CZ 281884	B6	19970312	CZ 1994-2505	19930421
ZA 9302855	A	19941024	ZA 1993-2855	19930422
IL 105555	A1	19980715	IL 1993-105555	19930429
CN 1079964	A	19931229	CN 1993-105039	19930508
CN 1044236	B	19990721		
US 5700799	A	19971223	US 1996-610031	19960304

PRIORITY APPLN. INFO.: US 1992-880432 B2 19920508
US 1994-332822 A3 19941031
OTHER SOURCE(S): MARPAT 125:221870
GI



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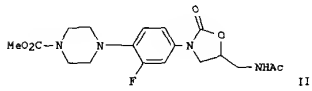


II

AB Title compds. I or pharmaceutically acceptable salts thereof wherein: each

L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

n is independently 1 to 3; Y is chosen from, e.g., (a) C(O)C1-6 alkyl,
C(O)OC1-6 alkyl or benzoyl, (b) N(R3)2 where R3 is independently hydrogen,
C1-4 alkyl or Ph which can be substituted with one to three F, Cl, OCH3,
OH, NH2, or C1-4 alkyl, wherein each occurrence of said C1-6 alkyl may be
substituted with one or more F, Cl, Br, I, OR1, CO2R1, CN, SR1, or R1
(where R1 is a hydrogen or C1-4 alkyl); X and Z are independently C1-6
alkyl, C3-12 cycloalkyl or hydrogen, or X and Z form a C0-3 bridging
group, preferably X and Z are hydrogen; U, V and W are independently C1-6
alkyl, F, Cl, Br, hydrogen or a C1-6 alkyl substituted with one or more
F, Cl, Br or I, preferably U and V are F and W is hydrogen; R is hydrogen,
C1-12 alkyl, C3-12 cycloalkyl, C1-6 alkoxy, C1-6 alkyl substituted with
one or more F, Cl, Br, I or OH; and q is 0 to 4 inclusive, are useful
antimicrobial agents, effective against a no. of human and veterinary
pathogens, including multiply-resistant staphylococci and streptococci, as
well as anaerobic organisms such as bacteroides and clostridia species,
and acid-fast organisms such as Mycobacterium tuberculosis and
Mycobacterium avium. Thus, e.g., arylation of piperazine with
3,4-difluoronitrobenzene afforded 1-(2-fluoro-4-nitrophenyl)piperazine;
Boc protection followed by redn. provided 1-(tert-butoxycarbonyl)-4-(2-
fluoro-4-aminophenyl)piperazine; the latter was converted to the Cbz
deriv. and then allylated to give 1-(tert-butoxycarbony1)-4-(2-fluoro-4-
benzyloxycarbonylallylamino)piperazine; dihydroxylation followed by
cyclization afforded 3-[3-fluoro-4-(4-tert-butoxycarbonylpiperazin-1-
yl)phenyl]-5-hydroxymethyl-2-oxazolidinone; the 5-hydroxymethyl group was
converted to a 5-acetylaminomethyl group by mesylation, azidification,
hydrogenation, and acetylation; finally, Boc deprotection followed by
treatment with MeO2CCl afforded oxazolidinone II which exhibited
antibacterial activity ED50 of 1.8 mg/kg PO against S. aureus vs. 1.8
mg/kg SC for vancomycin, and 2.3 mg/kg PO against S. pyogenes vs. 2.6
mg/kg SC for clindamycin.

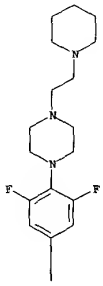
IT **154590-81-5P 154590-90-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
((piperazinylphenyl)oxazolidinone antimicrobials)

RN 154590-81-5 CAPLUS
CN Acetamide, N-[[3-(3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

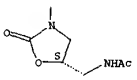
L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

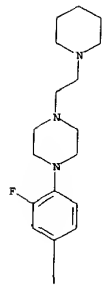


RN 154590-90-6 CAPLUS
CN Acetamide, N-[[3-[3-fluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

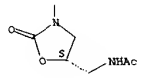
Absolute stereochemistry.

L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A



PAGE 2-A



L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:435300 CAPLUS
DOCUMENT NUMBER: 125:104287
TITLE: Structure activity relationships of a series of buspirone analogs at alpha-1 adrenoceptors: further evidence that rat aorta alpha-1 adrenoceptors are of the alpha-1D-subtype
AUTHOR(S): Saussy, David L., Jr.; Goetz, Aaron S.; Queen, Kennedy L.; King, Holly K.; Lutz, Michael W.; Rimele, Thomas J.
CORPORATE SOURCE: Dep. Receptor Biochem., Glaxo Welcome, Inc., Research Triangle Park, NC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 278(1), 136-144
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

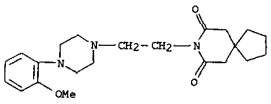
AB The activity of a series of buspirone analogs at recombinant and rat thoracic aorta alpha-1 adrenoceptors was investigated. Compd. affinity for recombinant alpha-1A, alpha-1B and alpha-1D adrenoceptors from human and animal sources was detd. by radioligand binding assays using membranes prepd. from rat-1 fibroblasts expressing recombinant receptors with (.+-.)-[125I]iodo-HEAT as the radioligand. Compd. affinity and functional activity at rat aortic alpha-1 adrenoceptors were detd. using endothelium denuded rings contracted with phenylephrine. BMY 7378 and MDL 73005EF were found to have significant selectivity for the alpha-1D-subtype and were high affinity antagonists of the alpha-1 adrenoceptors in the rat aorta. Leverage plot anal. of affinities of the buspirone analogs and a series of structurally diverse alpha-1 antagonists for recombinant alpha-1 adrenoceptors and rat aorta alpha-1 adrenoceptors demonstrate that the alpha-1 adrenoceptors in the rat aorta are predominantly of the alpha-1D subtype.

IT **21102-95-4**, BMY 7378 **25024-76-4 179388-69-3**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure activity relationships of buspirone analogs at .alpha.1-adrenoceptors and characterization of rat aorta .alpha.1-adrenoceptors as .alpha.1D subtype)

RN 21102-95-4 CAPLUS

L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

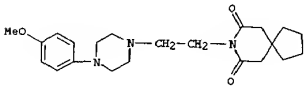
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 25024-76-4 CAPLUS

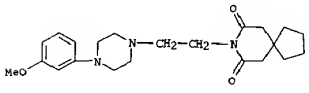
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 179388-69-3 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS

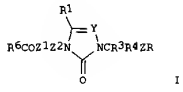
ACCESSION NUMBER: 1996:252231 CAPLUS
DOCUMENT NUMBER: 124:289578
TITLE: Preparation of N-[[4-(alkanoyl- and aroyl)piperazino]pyridyl]triazolones and analogs as anti-Helicobacter agents
INVENTOR(S): Heeres, Jan; Stokbroekx, Raymond Antoine; Mostmans, Joseph Hector; Van Der Veken, Louis Jozef Elis
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601822	A1	19960125	WO 1995-EP2618	19950705
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5637592	A	19970610	US 1995-448082	19950523
CA 2193490	AA	19960125	CA 1995-2193490	19950705
AU 9530757	A1	19960209	AU 1995-30757	19950705
AU 685310	B2	19980115		
EP 770074	A1	19970502	EP 1995-926392	19950705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1152311	A	19970618	CN 1995-194023	19950705
CN 1071331	B	20010919		
BR 9508377	A	19971028	BR 1995-8377	19950705
HU 76638	A2	19971028	HU 1997-76	19950705
JP 10502385	T2	19980303	JP 1995-504111	19950705
RU 2152392	C1	20000710	RU 1997-102153	19950705
ZA 9505759	A	19970113	ZA 1995-5759	19950711
IL 114536	A1	19990411	IL 1995-114536	19950711
NO 9700088	A	19970310	NO 1997-88	19970109
FI 9700112	A	19970110	FI 1997-112	19970110

PRIORITY APPLN. INFO.: EP 1994-202019 A 19940712
WO 1995-EP2618 W 19950705

OTHER SOURCE(S): MARPAT 124:289578
GI

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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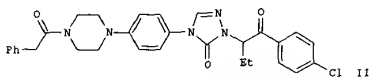


II

AB Title compds. [I; R = (un)substituted Ph; R1-R3 = H, alkyl; R6 = (cyclo)alkyl, (hetero)aryl, etc.; Y = CH or N; Z = CO, CH(OH); Z1 = piperazine-1,4-di-yl; Z2 = 1,4-phenylene, pyridine-2,5-di-yl, pyrimidine-2,5-di-yl] were prepd. Thus, title compd. II had MIC of .ltoreq.1.mu.M against Helicobacter pylori in vitro.

IT **175715-52-3P 175715-53-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-[[4-(alkanoyl- and aroyl)piperazino]pyridyl]triazolones and analogs as anti-Helicobacter agents)

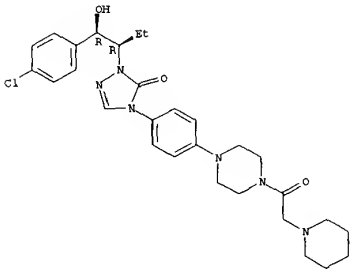
RN 175715-52-3 CAPLUS

CN Piperazine, 1-[4-[1-[1-[(4-chlorophenyl)hydroxymethyl]propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-4-(1-piperidinylacetyl)-, (R*,R*)-

(9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 175715-53-4 CAPLUS

CN Piperazine, 1-[4-[1-[1-(4-chlorobenzoyl)propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)

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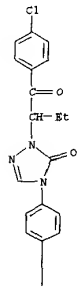

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

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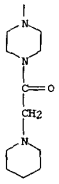


L14 ANSWER 122 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:190223 CAPLUS

DOCUMENT NUMBER: 124:306509

TITLE: 2-[4-(o-Methoxyphenyl)piperazin-1-ylmethyl]-1,3-dioxoperhydroimidazo[1, 5-a]pyridine as a new selective 5-HT1A receptor ligand

AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose; Rosado, M. Luisa; Benhamu, Bellinda; Sanz, Antonio M.

CORPORATE SOURCE: Fac. Ciencias Quimicas, Univ. Complutense, Madrid, 28040, Spain

SOURCE: Bioorg. Med. Chem. Lett. (1996), 6(6), 689-94
CODEN: BMCLE8; ISSN: 0960-894X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 124:306509

AB A series of 2-[.omega.-(4-arylpiperazin-1-yl)alkyl]-1,3-dioxoperhydroimidazo[1,5-a]pyridine derivs. was prepd. and evaluated for affinity at 5-HT1A and .alpha.1 receptors. The most promising analog bound at 5-HT1A sites with nanomolar affinity (Ki = 31.7) and high selectivity over .alpha.1, D2 and 5-HT2.alpha. receptors (Ki > 1000, Ki > 10 000, Ki > 1000 nM, resp.). Preliminary studies showed that this agent is a presynaptic 5-HT1A agonist, and it displayed activity in the face to face behavioral model.

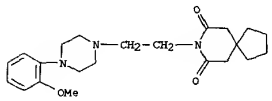
IT **21102-94-3**

RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)

(prepn. of dioxoperhydroimidazopyridine derivs. as new selective serotoninergic S1A receptor ligands in relation to agonist activity and structure)

RN 21102-94-3 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

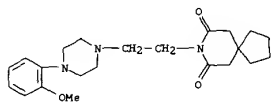


L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:95589 CAPLUS
DOCUMENT NUMBER: 124:232163
TITLE: 8-[4-[2-(1,2,3,4-Tetrahydroisoquinolinyl)]butyl]-8-azaspiro[4.5]decane-7,9-dione: A New 5-HT1A Receptor Ligand with the Same Activity Profile as Buspirone
AUTHOR(S): Mokrosz, Jerzy L.; Deren-Wesolek, Anna; Tatarczynska, Ewa; Duszynska, Beata; Bojarski, Andrzej J.; Mokrosz, Maria J.; Chojnacka-Wojcik, Ewa
CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
SOURCE: Journal of Medicinal Chemistry (1996), 39(5), 1125-9
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new analog of buspirone, i.e., 8-[4-[2-(1,2,3,4-tetrahydroisoquinolinyl)]butyl]-8-azaspiro[4.5]decane-7,9-dione (6a), was synthesized. It was demonstrated that buspirone and its analog 6a were equipotent 5-HT1A ligands. Several behavioral models showed that 6a had essentially the same functional profile at 5-HT1A receptors as buspirone. The obtained results permit a conclusion that the basic nitrogen atom and terminal, bulky cycloimide moiety, but not the 2-pyrimidinyl group, of buspirone are directly involved in the formation of the bioactive complex with 5-HT1A receptors.

IT **21102-94-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(activity as a 5-HT1A receptor ligand)
RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NANE)

L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

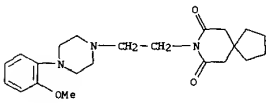


L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 20D2 ACS
ACCESSION NUMBER: 1996:18915 CAPLUS
DOCUMENT NUMBER: 124:46391
TITLE: The specific contribution of the novel alpha-1D adrenoceptor to the contraction of vascular smooth muscle
AUTHOR(S): Piascik, Michael T.; Guarino, Richard D.; Smith, Marta S.; Soltis, Edward E.; Saussy, David L., Jr.; Perez, Dianne M.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Kentucky, Lexington, KY, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 275(3), 1583-8
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB With a selective antagonist, the specific contribution of the alpha-1D adrenoceptor (AR) to vascular smooth muscle contraction has been assessed. BMY 7378 bound to membranes expressing the cloned rat alpha-1D AR with a >100-fold higher affinity (Ki = 2 nM) than binding to either the cloned rat alpha-1A AR (Ki = 800 nM) or the hamster alpha-1B AR (Ki = 600 nM). BMY 7378 exhibited differential potency in inhibiting vascular smooth muscle contraction. In the rat aorta and iliac artery, BMY 7378 was a high-affinity antagonist, producing parallel shifts in the phenylephrine concn.-response curve. The dissocn. consts. for this compd. by Schild anal. were 0.95 and 4 nM for the aorta and iliac artery, resp. The slopes of these Schild plots were not significantly different from unity. BMY 7378 was a weak antagonist in the rat caudal, mesenteric resistance and renal arteries, with Schild slopes significantly <1. With RNase protection assays, alpha-1D mRNA was found in all blood vessels examd. These data suggest that (1) BMY 7378 is a selective alpha-1D AR antagonist that can be used in functional systems to assess the contribution of this receptor in vascular smooth muscle contraction; (2) the alpha-1D AR appears to play a major role in the contraction of the aorta and iliac artery; (3) despite the fact that the mRNA for the alpha-1D AR can be detected in the caudal, mesenteric resistance and renal arteries, it does not appear to play a role in mediating contraction of these blood vessels; and (4) expression of alpha-1D mRNA in a particular artery does not ensure that this receptor is involved in regulating the contraction of that artery.

L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

IT **21102-95-4**, BMY 7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(.alpha.1D-adrenoceptor-mediated vascular smooth muscle contraction antagonism by BMY 7378)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:916470 CAPLUS
DOCUMENT NUMBER: 123:314021
TITLE: Preparation of piperazine-substituted pyrroloanthracenes as immunomodulators.
INVENTOR(S): Schwenner, Eckhard; Ladouceur, Gaeton; Kabbe, Hans-Joachim; Aune, Thomas Martin
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

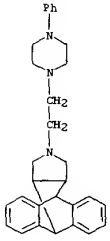
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9515946	A1	19950615	WO 1994-EP3934	19941128
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5409932	A	19950425	US 1993-164499	19931209
US 5459143	A	19951017	US 1993-164509	19931209
AU 9512411	A1	19950627	AU 1995-12411	19941128
EP 733040	A1	19960925	EP 1995-903294	19941128
R: CH, DE, FR, GB, IT, LI				
JP 09506356	T2	19970624	JP 1994-515934	19941128

PRIORITY APPLN. INFO.: US 1993-164499 19931209
US 1993-164509 19931209
WO 1994-EP3934 19941128
OTHER SOURCE(S): MARPAT 123:314021
GI

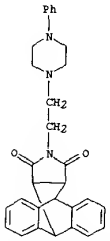
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; A, D = H, OH, halo, cyano, CO2H, NO2, CF3, OCF3, alkyl, alkoxy; R1, R2 = H, halo, cyano, CHO, Ph, OH, (substituted) alkyl, alkenyl; R5, R6 = H, halo, Ph, (substituted) alkyl; R7-R10 = H, alkyl; R7R8, R9R10 = O; a = 2-8; R11 = H, cycloalkyl, pyridyl, pyrimidinyl, (substituted) aryl, alkyl], were prepd. Thus, 9,10-dihydro-9,10[3',4']-furanoanthracene-12,14(11H,15H)-dione (prepn. given) was refluxed with 3-[4-(4-fluorophenyl)piperazin-1-yl]propylamine (prepn. given) in xylene using a water separator to give 98% title compd. (II). At 10 mg/kg i.p. in rats, I gave 4-90% inhibition of paw swelling in the adjuvant arthritis

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



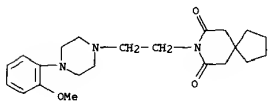
L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
model.
IT **169877-38-7P 169877-92-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine-substituted pyrroloanthracenes as immunomodulators)
RN 169877-38-7 CAPLUS
CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole-1,3(2H)-dione, 3a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 169877-92-3 CAPLUS
CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole, 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

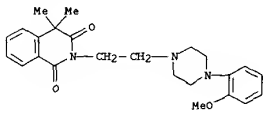
L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:882567 CAPLUS
DOCUMENT NUMBER: 123:329777
TITLE: Effects of the NMDA antagonist, dizocilpine, in various drug discriminations: characterization of intermediate levels of drug lever selection
AUTHOR(S): Koek, W.; Kleven, M.S.; Colpaert, F.C.
CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
SOURCE: Behav. Pharmacol. (1995), Volume Date 1995, 6(5 & 6), 590-600
CODEN: BPHAEL; ISSN: 0955-8810
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In each of different groups of rats trained to discriminate either 8-OH-DPAT, DOI, d-amphetamine, cocaine, chlordiazepoxide, or ethanol from saline, dizocilpine produced max. percentages of drug lever (DL) selection that were intermediate between those produced by the training conditions. Dizocilpine also decreased DL selection produced by the training dose in each of the discriminations, except in ethanol-trained rats. In all discriminations, with the exception of ethanol-trained rats, the intermediate levels of DL selection produced by dizocilpine were assocd. with increased FRF values (sum of the responses made on either lever before the first reinforcement occurred), increased lever selection latencies, and increased responding on the nonselected lever. At doses that, in general, had effects on response rate similar to those of dizocilpine, intermediate levels of DL selection were produced by BMY 7378 in 8-OH-DPAT-trained rats, by WY 50,324 in DOI-trained rats, by (-)-3-PPP in d-amphetamine- and in cocaine-trained rats, by alpidem in chlordiazepoxide-trained rats, and by PCP in ethanol-trained rats. The intermediate levels of DL selection produced by these latter drugs were not assocd. with simultaneous increases of FRF values, selection latencies, and responding on the nonselected lever. The results suggest that dizocilpine produces intermediate levels of drug-appropriate responding through the behavioral mechanism of partial generalization only in ethanol-trained rats; in all other discriminations examd. here, the effects of dizocilpine appear to involve (1) pharmacol. effects that differ from those of the training drug, and (2) behavioral mechanisms that are unrelated to stimulus generalization. The differentiation of partial generalization and other mechanisms whereby intermediate responding can occur in the drug discrimination paradigm requires analyses that are more

L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
detailed than those commonly used in drug discrimination research.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of the NMDA antagonist, dizocilpine, in various drug discriminations: characterization of intermediate levels of drug lever selection)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



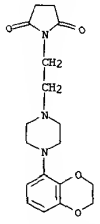
●2 HCl

L14 ANSWER 127 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:828929 CAPLUS
DOCUMENT NUMBER: 123:275756
TITLE: Identification of drugs subtype-selective for .alpha.2A-, .alpha.2B-, and .alpha.2C-adrenoceptors in the pig cerebellum and kidney cortex
AUTHOR(S): Wikberg-Matsson, Anna; Wikberg, Jarl E. S.; Uhlen, Staffan
CORPORATE SOURCE: Department of Ophthalmology, Academic Hospital, Uppsala, Swed.
SOURCE: Eur. J. Pharmacol. (1995), 284(3), 271-9
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The radioligands [3H]MK912 and [3M]RX821002 were used to label .alpha.2A-, .alpha.2B-, and .alpha.2C-adrenoceptors of the pig cerebellum and kidney cortex. By inclusion of the .alpha.2A-adrenoceptor-selective drug, BRL44408, and using a 'multi-curve' exptl. design all the three porcine .alpha.2-adrenoceptor subtypes could be characterized pharmacol. The data indicate that the pig .alpha.2-adrenoceptor subtypes are pharmacol. more related to human .alpha.2-adrenoceptor subtypes than to the rodent .alpha.2-adrenoceptors. The authors suggest a set of drugs that are useful for the delineation of the pig .alpha.2-adrenoceptor subtypes.
IT **67339-62-2**, ARC239
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(identification of drugs subtype-selective for .alpha.2A-, .alpha.2B-, and .alpha.2C-adrenoceptors in the pig cerebellum and kidney cortex)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

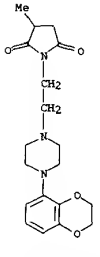


L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:826862 CAPLUS
DOCUMENT NUMBER: 124:55875
TITLE: A Series of N4-Imidoethyl Derivatives of 1-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazine as 5-HT1A Receptor Ligands: Synthesis and Structure-Affinity Relationships
AUTHOR(S): van Steen, B. J.; van Wijngaarden, I.; Tulp, M. Th.; Soudijn, W.
CORPORATE SOURCE: Department of Medicinal Chemistry, Solvay Duphar Research Laboratories, Weesp, 1380 DA, Neth.
SOURCE: Journal of Medicinal Chemistry (1995), 38(21), 4303-8
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of unsubstituted and substituted succinimido, maleimido, and glutarimidoethyl derivs. of eltoprazine was synthesized and tested for affinity for the 5-HT1A receptor in rat brain homogenates. The unsubstituted compds. have a moderate affinity for the receptor, while the affinity considerably increases by substitution at or enlargement of these cyclic ring systems. A good correlation was found between the inhibition const. Ki (expressed as pKi) and the lipophilicity (clogP). No correlation was obsd. between the pKi or pKi+ (local inhibition const.) and the basicity of the N4-nitrogen atom.
IT **171877-00-2P 171877-01-3P 171877-02-4P**
171877-03-5P 171877-08-0P 171877-09-1P
171877-10-4P 171877-11-5P 171877-13-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure-affinity relationships of N4-imidoethyl derivs. of (Dihydrobenzodioxinyl]piperazine)
RN 171877-00-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

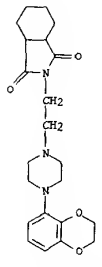
L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 171877-01-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-3-methyl- (9CI) (CA INDEX NAME)

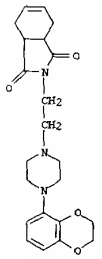


RN 171877-02-4 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]hexahydro-, dihydrochloride (9CI) (CA INDEX NAME)



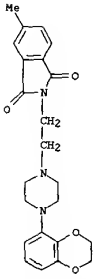
●2 HCl

RN 171877-03-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)

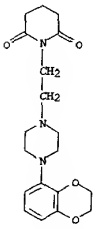


●2 HCl

RN 171877-08-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-



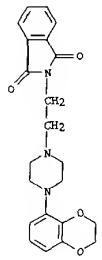
RN 171877-10-4 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 171877-11-5 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

CM 1

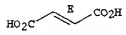
CRN 171877-07-9
CMF C22 H23 N3 O4



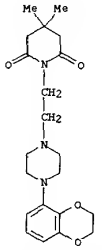
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 171877-09-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-5-methyl- (9CI) (CA INDEX NAME)

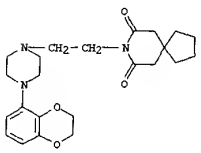


●2 HCl

RN 171877-13-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione,
8-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

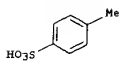
CRN 171877-12-6
CMF C23 H31 N3 O4



CM 2

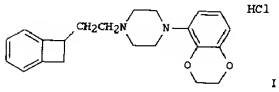
CRN 104-15-4
CMF C7 H8 O3 S

L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:790900 CAPLUS
DOCUMENT NUMBER: 124:134742
TITLE: Characterization of Potent and Selective Antagonists at Postsynaptic 5-HT1A Receptors in a Series of N4-Substituted Arylpiperazines
AUTHOR(S): Peglion, Jean-Louis; Canton, Herve; Bervoets, Karin; Audinot, Valerie; Brocco, Mauricette; Gobert, Alain; Le Marouille-Girardon, Sylvie; Millan, Mark J.
CORPORATE SOURCE: Institut de Recherches Servier, Suresnes, 92150, Fr.
SOURCE: Journal of Medicinal Chemistry (1995), 38(20), 4044-55
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

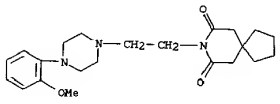
AB Benzocycloalkyl and benzocycloalkenyl moieties linked, directly or via an alkyl chain, to oxygen-bearing heteroarylpiperazines were synthesized, in an attempt to obtain potent and selective antagonists at postsynaptic 5-HT1A receptors. From the numerous arylpiperazines described in the literature, 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazine was chosen as a model of an arylpiperazine in view of its selectivity for 5-HT1A receptors vs. .alpha.1-, .alpha.2-, and .beta.-adrenergic receptors, as well as dopamine D1 and D2 receptors. Two other closely-related arylpiperazines, 1-(1,5-benzodioxepin-6-yl)piperazine and 1-(benzofuran-7-yl)piperazine, were also examd. in this study. All compds. showed high affinity at 5-HT1A sites (8.10 .ltoreq. pKis < 9.35), and the majority behaved as antagonists in vivo in blocking the hypothermia induced by the 5-HT1A agonist 8-OH-DPAT in the absence of a marked effect alone at equiv. doses. An in vivo evaluation of dopamine D2 receptor antagonist properties revealed that the majority of compds. was devoid of activity at this site,

L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

in marked contrast to BMY 7378 which displayed virtually no selectivity for 5-HT1A vs. dopamine D2 receptors. Moreover, six compds. of the present series, including I, showed >10-fold selectivity in vitro for 5-HT1A vs. .alpha.1-adrenergic receptors. I displayed an optimal compromise between potency (pKi = 8.75), marked antagonist activity, and selectivity toward .alpha.1-adrenergic (81-fold) and dopamine D2 195-fold receptors. These characteristics clearly distinguish I from previously-reported ligands such as the postsynaptic 5-HT1A antagonist BMY 7378 and the weak partial agonist NAN 190 which, in contrast to the compds. of this series, belong to the well-exemplified class of imido derivs. of (o-methoxyphenyl)piperazines. The availability of I (S 15535) should facilitate the further elucidation of the functional role and potential therapeutic significance of 5-HT1A receptors.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(potent and selective antagonists at postsynaptic 5-HT1A receptors in a series of N4-substituted arylpiperazines)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 130 OF 263 CAPLUS COPYRIGHT 2002 ACS

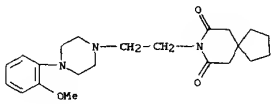
ACCESSION NUMBER: 1995:698387 CAPLUS
DOCUMENT NUMBER: 123:103264
TITLE: Studies on the role of 5-HT1A autoreceptors and .alpha.1-adrenoceptors in the inhibition of 5-HT release. I. BMY7378 and prazosin
AUTHOR(S): Hjorth, S.; Bengtsson, H. J.; Milano, S.; Lundberg, J.F.; Sharp, T.
CORPORATE SOURCE: Dep. Pharmacology, Univ. Goeteborg, Goeteborg, 413 90, Swed.
SOURCE: Neuropharmacology (1995), 34(6), 615-20
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study utilized in vivo microdialysis to investigate the importance of 5-HT1A autoreceptors and .alpha.1-adrenoceptors in the decreased 5-HT release obtained following administration of the mixed 5-HT1A autoreceptor partial agonist/.alpha.1-adrenoceptor antagonist BMY 7378, the selective 5-HT1A receptor agonist 8-OH-DPAT and the .alpha.1-adrenoceptor antagonist prazosin. BMY 7378 (0.25 mg/kg, s.c.), 8-OH-DPAT (0.025 mg/kg, s.c.) and prazosin (0.1-1.0 mg/kg, s.c.) all suppressed ventral hippocampal 5-HT efflux. The BMY 7378- and 8-OH-DPAT-induced inhibition of 5-HT release were reversed by a 40 min pretreatment with either (.+-.)pindolol (8 mg/kg, s.c.) or WAY-100635 (0.3 mg/kg, s.c.), to block 5-HT1A autoreceptors. Neither of these antagonists altered the prazosin-induced (0.3 mg/kg, s.c.) 5-HT decrease. The results: (i) confirm that both an .alpha.1-adrenoceptor antagonist (prazosin) and 5-HT1A autoreceptor stimulants (BMY 7378 and 8-OH-DPAT) may reduce cerebral 5-HT release; (ii) support that the BMY 7378-induced decrease in 5-HT release results from 5-HT1A autoreceptor agonism, rather than .alpha.1-adrenoceptor blockade; and (iii) argue against "physiol." antagonism (i.e. via blockade of .beta.-adrenoceptors, 5-HT1B receptors or some other mechanism) as an explanation for the reversal by pindolol of 5-HT1A autoreceptor agonist-induced suppression of 5-HT release. These data support the usefulness of pindolol, as well as the more specific compd. WAY-100635, to block 5-HT1A autoreceptors.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(5-HT1A autoreceptors and .alpha.1-adrenoceptors in inhibition of hippocampal 5-HT release)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 130 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:644351 CAPLUS
DOCUMENT NUMBER: 123:26183
TITLE: Modulation of the activity of central serotoninergic neurons by novel serotonin1A receptor agonists and antagonists: a comparison to adrenergic and dopaminergic neurons in rats
AUTHOR(S): Gobert, A.; Lejeune, F.; Rivet, J.-M.; Audinot, V.; Newman-Tancredi, A.; Millan, M. J.
CORPORATE SOURCE: Dep. of Psychopharmacology, Inst. Recherches Servier, Croissy-sur-Seine, 78290, Fr.
SOURCE: J. Pharmacol. Exp. Ther. (1995), 273(3), 1032-46
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, the authors used a complementary in vivo electrophysiol. and (in individual rats) neurochem. approach to characterize the actions of chem. diverse serotonin (5-HT)1A receptor ligands at central 5-HT1A autoreceptors as compared to dopamine (DA) D2 autoreceptors and presynaptic alpha-2 adrenergic receptors (ARs). The novel, high efficacy, 5-HT1A agonists, WY 48,723 (an arylpiperazine), (+)-flesinoxan (a benzodioxane) and S 14671 and S 14506 (methoxynaphthylpiperazines) mimicked the aminotetralin, 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide (8-OH-DPAT), in inhibiting the firing of dorsal raphe nucleus (DRN) neurons. Similarly, the firing rate of DRN neurons was reduced by the "partial" agonists, MDL 73005EF, BMY 7378, NAN-190, tandospirone and the novel pyrimidinylpiperazine, zalospirone. Furthermore, S 14489, S 15535 and S 15931, novel benzodioxopiperazines, which behave as antagonists at postsynaptic 5-HT1A receptors, inhibited completely DRN firing, whereas the methoxyphenylpiperazine, WAY 100,135, and the aryloxyarylamine, (-)-tertatolol, were ineffective. Indeed, in analogy to spiperone, both WAY 100,135 and (-)-tertatolol behaved as apparently competitive antagonists in that, in their presence, the dose-response curves for inhibition of DRN firing by S 14671, S 14506 or 8-OH-DPAT were shifted in parallel to the right with no loss of maximal effect. In distinction to WAY 100,135 and (-)-tertatolol, a further novel, putative "antagonist," SDZ 216-525 (a benzoisothiazolpiperazine) weakly inhibited the elec. activity of the DRN. With the exception of (-)-tertatolol, which behaved as a weak agonist, a very similar pattern of inhibition of 5-HT turnover was seen in the striatum (innervated by the DRN), the hippocampus and the hypothalamus (DRN and median raphe nucleus) and the spinal cord (nucleus raphe magnus), with the striatum displaying the

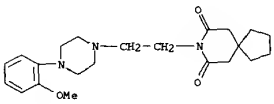
L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

greatest sensitivity. Drug potency for inhibition of firing and turnover was highly correlated (r = 0.80-0.82) and these actions were significantly correlated to affinity at (hippocampal) 5-HT1A receptors (r = 0.62-0.73). As concerns DA D2 autoreceptors, the agonist action of apomorphine in reducing DA turnover were mimicked only by 8-OH-DPAT, whereas the majority of the other 5-HT1A ligands, in analogy to raclopride, enhanced DA turnover. The facilitation of DA turnover appeared to reflect direct blockage of DA D2 autoreceptors because potency was correlated powerfully to affinity at these D2 sites (r = 0.89). None of the 5-HT1A ligands mimicked the agonist action of clonidine at alpha-2 AR autoreceptors, whereas the turnover-enhancing actions of the alpha-2 AR antagonists, idazoxan and 1-(2-pyrimidinyl)piperazine, were mimicked by many 5-HT1A ligands. Their potency did not, however, correlate with their affinity at alpha-2 ARs (r = 0.13), probably because the alpha-2 AR antagonist actions of several ligands reflect their metab. to 1-(2-pyrimidinyl)piperazine. In conclusion, in addn. to their agonist or antagonist actions at central 5-HT1A autoreceptors, many 5-HT1A ligands display pronounced in vivo actions at presynaptic DA D2 receptors and alpha-2 ARs. Nevertheless, several ligand, such as S 14671, (+)-flesinoxan, S 15535 and WAY 100,235, display marked selectivity for 5-HT1A autoreceptors and an evaluation of their potential therapeutic properties should prove of particular interest.

IT 21102-95-4, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(modulation of the activity of central serotoninergic neurons by novel serotonin1A receptor agonists and antagonists)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

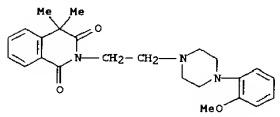
L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:622064 CAPLUS
DOCUMENT NUMBER: 123:47330
TITLE: Comparison of the binding activities of some drugs on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in the guinea pig
AUTHOR(S): Uhlen, Staffan; Muceniece, Ruta; Rangel, Ninfa; Tiger, Gunnar; Wikberg, Jarl E. S.
CORPORATE SOURCE: Dep. Pharmacology, Umea Univ., Umea, S-901 87, Swed.
SOURCE: Pharmacol. Toxicol. (Copenhagen) (1995), 76(6), 353-64
CODEN: PHTOEH; ISSN: 0901-9928
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Simultaneous computer modeling of control and guanfacine-masked [3H]-MK 912 satn. curves as well as guanfacine competition curves revealed that both .alpha.2A- and .alpha.2C-adrenoceptor subtypes were present in the guinea pig cerebral cortex. The Kd value of [3H]-MK 912 detd. for the .alpha.2A-subtype was 403 pM and for the .alpha.2C-subtype 79.8 pM; the receptor sites showing capacities 172 and 19.5 fmol/mg protein, resp. The KdS of guanfacine were 20 and 880 nM for the .alpha.2A- and .alpha.2C-adrenoceptor, resp. In the guinea pig kidney [3H]-MK 912 bound to a single saturable site with Kd 8.34 nM and capacity 285 fmol/mg protein, the site showing pharmacol. properties like an .alpha.2B-adrenoceptor. Binding consts. of 22 compds. for the three guinea pig .alpha.2-adrenoceptor subtypes were detd. by computer modeling competition curves using for the cerebral cortex a "3-curve assay", for the kidney an "1-curve assay", and using [3H]-MK 912 as labeled ligand. Of the tested drugs guanfacine and BRL 4408 were found to be clearly .alpha.2A-selective. Spiroxatrine, yohimbine, rauwolscine and Wb 4101, as well as [3H]-MK 912 itself, were found to be .alpha.2C-selective. The most selective compds. for .alpha.2B-adrenoceptors, when compared to .alpha.2A-adrenoceptors, were ARC 239 and prazosin. In the guinea pig kidney [3H]-p-aminoclonidine bound to .alpha.2-adrenoceptors as well as to non-adrenergic imidazoline sites. The .alpha.2-adrenoceptors could be completely blocked using 10 .mu.M (-)-adrenaline without the non-adrenergic sites being affected. During these conditions the anal. of

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
combined satn. and competition studies using labeled and unlabeled p-aminoclonidine with computer modeling revealed that the ligand labeled two different sites with KdS of 310 and 47,000 nM, resp. Competition curves of 16 compds. for the non-adrenergic [3H]-p-aminoclonidine sites were shallow and resolved into two-site fits. For the high affinity [3H]-p-aminoclonidine site the highest affinities were shown by 1-medetomidine, UK-14,304, guanabenz and detomidine; the KdS of these drugs ranging 26-72 nM. All drugs tested showed low but varying affinities for the low affinity [3H]-p-aminoclonidine site. These data indicated that the [3H]-p-aminoclonidine binding sites of the guinea pig kidney are grossly different from the [3H]-idazoxan binding I2-receptors previously demonstrated also to be present in the guinea pig kidney.
IT **67339-62-2**, ARC 239
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(comparison of drug binding on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in guinea pig)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:604026 CAPLUS
DOCUMENT NUMBER: 123:314014
TITLE: Preparation of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators
INVENTOR(S): Schwenner, Eckhard; Ladouceur, Gaetan; Kabbe, Hans-joachim; Aune, Thomas M.
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

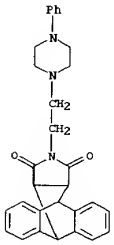
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5409932	A	19950425	US 1993-164499	19931209
WO 9515946	A1	19950615	WO 1994-EP3934	19941128
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9512411	A1	19950627	AU 1995-12411	19941128
EP 733040	A1	19960925	EP 1995-903294	19941128
R: CH, DE, FR, GB, IT, LI				
JP 09506356	T2	19970624	JP 1994-515934	19941128

PRIORITY APPLN. INFO.: US 1993-164499 19931209
US 1993-164509 19931209
WO 1994-EP3934 19941128
OTHER SOURCE(S): MARPAT 123:314014
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

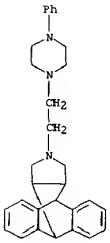
AB The title compds. [I; A, D = H, OH, halogen, CN, CO2H, NO2, CF3, CF3O, (un)branched C.ltoreq.8 alkyl or alkoxy; R1, R2 = H, halogen, CN, CHO, Ph, OH, (un)substituted alkoxy, (un)substituted alkyl, (un)substituted alkenyl; R3, R4 = H, C.ltoreq.6 (un)branched alkyl, Ph; R5, R6 = H, halogen, Ph, (un)branched (un)substituted alkyl; R7-R10 = H, C.ltoreq.6 (un)branched alkyl; R11 = (un)substituted aryl; a = 0-6] (e.g., II), useful as antiinflammatories, antiarthritics, and immunosuppressants, are prepd. Thus, II, m.p. 143.degree., was prepd. and demonstrated 90% inhibition of swelling in an adjuvant arthritis rat model at 10 mg/kg (i.p.).
IT **169877-38-7P 169877-92-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators)
RN 169877-38-7 CAPLUS
CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole-1,3(2H)-dione, 3a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

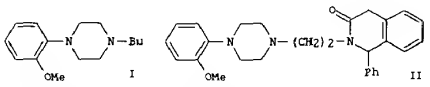


RN 169877-92-3 CAPLUS
CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole, 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

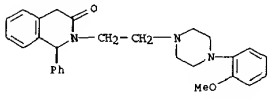


L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:540324 CAPLUS
DOCUMENT NUMBER: 123:74214
TITLE: Structure-activity relationship studies of CNS agents.
XXI: Two derivatives of 1-(o-methoxyphenyl)piperazine with an opposite function at 5-HT1A receptors
AUTHOR(S): Mokrosz, Jerzy L.; Klodzinska, Aleksandra; Boksa, Jan; Bojarski, Andrzej J.; Duszynska, Beata; Chojnacka-Wojcik, Ewa
CORPORATE SOURCE: Dep. Med. Chem., Lab. New Drugs Inst. Pharmacology, Polish Acad. Sci., Krakow, 31-343, Pol.
SOURCE: Arch. Pharm. (Weinheim, Ger.) (1995), 328(4), 381-3
CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



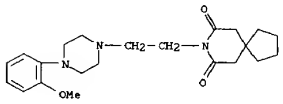
AB All postsynaptic 5-HT1A receptor antagonists which belong to the 1-arylpiperazine class of ligands have a 1-(o-methoxyphenyl)piperazine fragment or its structural equiv. (e.g.benzodioxane moiety) in their structure. Mol. modeling and structure activity studies were conducted by using model compds. I and II to substantiate the hypothesis that 1-(o-methoxyphenyl)piperazine moiety is necessary for the 5-HT1A receptor antagonist activity. Comparison of the 5-HT1A/5-HT2A selective ratio for I and II shows that the structure of the bioactive complex of I with 5-HT1A receptors is different form the 5-HT1A receptor complex of II. The 1-Ph, and not the 1-(o-methoxyphenyl), substituent and the N-4 piperazine atom of II form a pharmacophore which is recognized by the receptor. It may be anticipated that the structure of the specific bioactive complex of 5-HT1A receptor and 1-(o-methoxyphenyl)piperazine fragment is directly responsible for postsynaptic antagonist activity of these derivs.
IT **164988-55-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(mol. modeling and structure activity relations of the 5-HT1A receptor antagonist (methoxyphenyl)piperazine derivs.)
RN 164988-55-0 CAPLUS
CN 3(2H)-Isoquinolinone, 1,4-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-1-phenyl- (9CI) (CA INDEX NAME)



L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:470109 CAPLUS
DOCUMENT NUMBER: 122:230666
TITLE: Conditioned ultrasonic distress vocalizations in adult male rats as a behavioral paradigm for screening anti-panic drugs
AUTHOR(S): Molewijk, H. E.; van der Poel, A. M.; Mos, J.; van der Heyden, J. A. M.; Olivier, B.
CORPORATE SOURCE: CNS Pharmacol., Solvay Duphar B.V., Weesp, 1380 DA, Neth.
SOURCE: Psychopharmacology (Berlin) (1995), 117(1), 32-40
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rats may produce ultrasonic vocalizations (USV) in threatening situations. USV of adult male rats in assocn. with aversive stimulation was evaluated as a screening method for anxiolytic drugs. The triazolobenzodiazepine alprazolam, the 5-HT uptake inhibitors fluvoxamine and clomipramine, the mixed 5-HT/NA uptake inhibitor imipramine, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, the partial 5-HT1A receptor agonists buspirone, ipsapirone and BMY 7378, the .alpha.2-adrenoceptor agonist clonidine and the .alpha.2-adrenoceptor antagonist yohimbine reduced conditioned USV. The classical benzodiazepines (BZD) diazepam and chlordiazepoxide were ineffective or had a very low potency to decrease USV. The partial BZD receptor agonists bretazenil, alpidem and zolpidem, the BZD receptor antagonist flumazenil, the NA uptake inhibitors desipramine and maprotiline, and the 5-HT3 receptor antagonist ondansetron had no effect on conditioned USV. The dopamine-D2 receptor antagonist haloperidol reduced USV at a very high dose. In sep. expts. the effects of these drugs on locomotor activity were assessed. There was, however, no direct relation between effects on motor behavior and USV. In conclusion, the sensitivity of conditioned USV to 5-HT uptake inhibitors and alprazolam vs. the insensitivity to classical benzodiazepines and NA uptake inhibitors provides a very interesting profile, which closely resembles the psychopharmacol. of panic disorder. Also the face validity of conditioned USV towards situational panic attacks is high. We therefore propose conditioned USV in adult male rats as a novel behavioral paradigm to screen for anti-panic drugs.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); THU

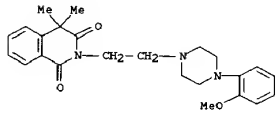
L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(Therapeutic use); BIOL (Biological study); USES (Uses)
(conditioned ultrasonic distress vocalizations in adult male rats as a
behavioral paradigm for screening antipanic drugs)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:466931 CAPLUS
DOCUMENT NUMBER: 122:230657
TITLE: Pharmacological antagonism of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo
AUTHOR(S): Brune, Michael E.; Buckner, Steven A.; Polakowski, James; Kerwin, James F., Jr.; Hancock, Arthur A.
CORPORATE SOURCE: Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, USA
SOURCE: Drug Dev. Res. (1995), 34(3), 267-75
CODEN: DDREDK; ISSN: 0272-4391
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment with .alpha.1 antagonists represents a pharmacol. alternative to surgery for the treatment of urinary obstruction assocd. with benign prostatic hyperplasia (BPH). A minimally invasive method to measure elevation of prostatic urethral tone through a urethral catheter was used to study the effects of .alpha.-adrenoceptor agonists and antagonists on canine intraurethral pressure (IUP). .alpha.1-Adrenoceptor agonists, but not .alpha.2 agonists, elicited elevations in IUP. The contractile response was primarily the result of prostatic smooth muscle contraction, since it was of smaller magnitude in female dogs or in male dogs outside of the prostatic urethra. The contractile responses to epinephrine obtained in the absence of antagonist on the same or different test dates were highly reproducible in dogs greater than 2 yr of age. The increase in IUP caused by epinephrine was specifically antagonized by .alpha.1-adrenoceptor antagonists, in direct proportion to their potency in isolated canine prostatic strips in vitro and in proportion to their affinity at receptors detd. in radioligand binding assays in vitro. These data confirm the role of .alpha.1-adrenoceptors in canine prostatic smooth muscle contraction and this relatively non-invasive in vivo model will allow the study of novel compds. for their effects on canine prostatic tone.
IT **67339-62-2**, AR-C 239
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. antagonism of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

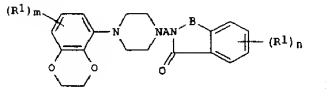


L14 ANSWER 137 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:422806 CAPLUS
DOCUMENT NUMBER: 122:187611
TITLE: Preparation of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivatives having 5-HT1a-antagonistic activity.
INVENTOR(S): Hartog, Jan; Van Steen, B. J.; Mos, Johannes; Schipper, Jacques
PATENT ASSIGNEE(S): Duphar International Research B.V., Neth.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

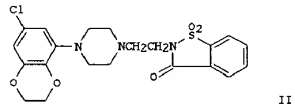
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 633260	A1	19950111	EP 1994-201900	19940701
EP 633260	B1	20011107		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2127084	AA	19950106	CA 1994-2127084	19940629
FI 9403149	A	19950106	FI 1994-3149	19940630
NO 9402471	A	19950106	NO 1994-2471	19940630
JP 07215972	A2	19950815	JP 1994-170370	19940630
US 5462942	A	19951031	US 1994-269086	19940630
HU 75155	A2	19970428	HU 1994-1965	19940630
HU 218215	B	20000628		
CZ 286503	B6	20000412	CZ 1994-1597	19940630
SK 281681	B6	20010611	SK 1994-788	19940630
ZA 9404787	A	19950220	ZA 1994-4787	19940701
CN 1106813	A	19950816	CN 1994-115999	19940701
CN 1044244	B	19990721		
AT 208385	E	20011115	AT 1994-201900	19940701
ES 2167346	T3	20020516	ES 1994-201900	19940701
AU 9466139	A1	19950112	AU 1994-66139	19940704
AU 680900	B2	19970814		
RU 2118322	C1	19980827	RU 1994-23250	19940704
IL 110209	A1	20000229	IL 1994-110209	19940704

PRIORITY APPLN. INFO.: EP 1993-201950 A 19930705
OTHER SOURCE(S): CASREACT 122:187611; MARPAT 122:187611
GI

L14 ANSWER 137 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



I

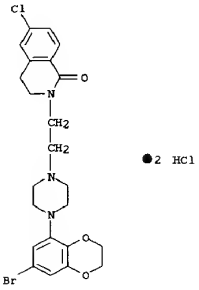


II

AB Title compds. (I; R1 = halo, lower alkyl, alkoxy, OH, CF3, cyano; m = 1,2;
n = 0,1; A = C2-6 alkylene which may be substituted with .gtoreq.1 lower
alkyl groups or a monocyclic (hetero)aryl group; B = CH2, CH2CH2, CO, S,
SO, SO2), were prepd. Thus, saccharin was heated with
1-(7-chloro-2,3-dihydro-1,4-benzodioxin-5-yl)-4-(2-chloroethyl)piperazine
and NaH in DMF to give title compd. (II). In general I were selective for
5-HT1a receptors, antagonize the effects of 8-OH-DPAT in rats, and have
good oral bioavailability.

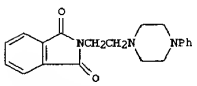
IT **161612-04-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(prepn. of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivs. having
5-HT1a-antagonistic activity)

RN 161612-04-0 CAPLUS
CN 1(2H)-Isoquinolinone,
2-[2-[4-(7-bromo-2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-6-chloro-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 138 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:376590 CAPLUS
DOCUMENT NUMBER: 122:214029
TITLE: Structure of N-[2-(4-phenyl-1-piperazinyl)ethyl]phthalimide
AUTHOR(S): Andronati, S. A.; Simonov, Yu. A.; Dvorkin, A. A.; Bondarev, M. L.; Yavorsky, A. S.; Chumakov, Yu. M.
CORPORATE SOURCE: Fiz.-Khim. Inst. im. A.V. Bogatskagi, Odessa, Ukraine
SOURCE: Dopov. Akad. Nauk Ukr. (1993), (11), 136-40
CODEN: DNUKEM
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI

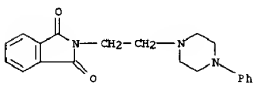


I

AB The structure of the title compd. (I) was detd. by x-ray anal. The distance from the center of the Ph ring to the center of the phthalimide
moiety was 9.90 .ANG.. This distance is comparable with that in Humber's
model for the dopamine receptor site. Quantum-chem. calcns., along with
x-ray data, confirm that the lone electron pair of N-4 of the piperazine
fragment is conjugated with the Ph ring.

IT **75000-24-7**
RL: PRP (Properties)
(x-ray anal. of)

RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
(CA INDEX NAME)

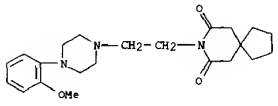


L14 ANSWER 139 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:320486 CAPLUS
DOCUMENT NUMBER: 122:97160
TITLE: BMY 7378 is a selective antagonist of the D subtype of
.alpha.1-adrenoceptors
AUTHOR(S): Goetz, Aaron S.; King, Holly K.; Ward, Stuart D. C.; True, Timothy A.; Rimele, Thomas J.; Saussy,, David L. Jr.
CORPORATE SOURCE: Department of Cellular Biochemistry, Glaxo Research
Institute, Five Moore Drive, Research Triangle Park,
NC, 27709, USA
SOURCE: Eur. J. Pharmacol. (1995), 272(2/3), R5-R6
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride), a 5-HT1A receptor partial
agonist, also binds to .alpha.1-adrenoceptors. Competition assays were
performed using (.+-.)-.beta.-([125I]iodo-4-hydroxyphenyl)-ethyl-aminomethyl-tetralone ([125I]HEAT), and membranes prepd. from Rat-1 fibroblasts expressing hamster .alpha.1b-, bovine .alpha.1c-, or rat .alpha.1d-adrenoceptor, or their resp. human homologues. Results indicate
that BMY 7378 is selective for the .alpha.1D-adrenoceptor subtype (pKi:
hamster .alpha.1b-adrenoceptor 6.2.+-.0.03, human .alpha.1b-adrenoceptor
7.2.+-.0.05; bovine .alpha.1c-adrenoceptor 6.1.+-.0.02, human .alpha.1c-adrenoceptor 6.6.+-.0.20; rat .alpha.1d-adrenoceptor 8.2.+-.0.06, human .alpha.1d-adrenoceptor 9.4.+-.0.05) and has high affinity (pA2, 8.9.+-.0.1) for rat aorta .alpha.1-adrenoceptor.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(BMY 7378 is selective antagonist of D subtype of .alpha.1-adrenoceptors)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

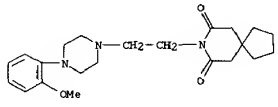
L14 ANSWER 139 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 140 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:252067 CAPLUS
DOCUMENT NUMBER: 122:24395
TITLE: Differential sensitivity of 3H-agonist binding to pre-
and postsynaptic 5-HT1A receptors in bovine brain
AUTHOR(S): Iben, Lawrence G.; Mahle, Cathy D.; Yocca, Frank D.
CORPORATE SOURCE: Psychobiol. Disorders, Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492, USA
SOURCE: Br. J. Pharmacol. (1994), 113(4), 1400-6
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The full and weak partial 5-HT1A agonist ligands [3H]-8-OH-DPAT and [3H]-BMY-7378 were used to characterize the binding parameters of pre- and postsynaptic 5-HT1A binding sites in bovine dorsal raphe and hippocampal membranes, resp. The Kd and Bmax values for the individual radioligands were indistinguishable across the regions tested, as were the Ki values generated by a series of agents acting at 5-hydroxytryptamine (5-HT) receptors. The concn.-dependent allosteric attenuation of [3H]-8-OH-DPAT and [3H]-BMY-7378 binding produced by the nonhydrolyzable guanyl nucleotide, Gpp(NH)p, generated similar IC50 values within a particular region; however, these were significantly different between regions. While the maximal attenuation of [3H]-8-OH-DPAT and [3H]-BMY-7378 binding was similar in dorsal raphe, Gpp(NH)p produced a significantly greater attenuation of [3H]-8-OH-DPAT binding in hippocampal membranes when compared to [3H]-BMY-7378. The maximal attenuation of [3H]-8-OH-DPAT binding by Gpp(NH)p in hippocampus was also significantly greater than that seen with either radioligand in dorsal raphe. Although exposure to Gpp(NH)p had no effect on the affinity consts. of either radioligand in either region, it produced a concn.-dependent redn. in the maximal no. of binding sites for both radioligands in both regions. While the percentage redn. in Bmax values were similar for both radioligands in the dorsal raphe, Gpp(NH)p reduced the Bmax of [3H]-8-OH-DPAT in the hippocampus significantly more than that of [3H]-BMY-7378. These results suggest that while pre- and postsynaptic 5-HT1A receptors may share similar pharmacol. recognition properties, a region-dependent difference in the coupling of the 5-HT1A receptor to G-proteins may exist.
IT **21102-95-4**, BMY-7378
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(serotonin pre- and postsynaptic S1A receptor ligand binding similarity

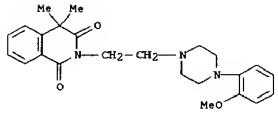
L14 ANSWER 140 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and region-dependent differences in G-protein coupling in brain)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 141 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:247986 CAPLUS
DOCUMENT NUMBER: 122:24361
TITLE: Species orthologs of the alpha-2A adrenergic receptor:
the pharmacological properties of the bovine and rat
receptors differ from the human and porcine receptors
AUTHOR(S): O'Rourke, M. F.; Iversen, L. J.; Lomasney, J. W.; Bylund, D. B.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Nebraska Med. Cent., Omaha, NE,
USA
SOURCE: J. Pharmacol. Exp. Ther. (1994), 271(2), 735-40
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Four pharmacol. subtypes of the alpha-2 adrenergic receptor have been identified; however, only three subtypes exist in any given species. Although the alpha-2A adrenergic receptor, as defined by the human platelet, and the alpha-2D receptor, as defined in the bovine pineal, have very different pharmacol. characteristics, they are more similar to each other than either is to the alpha-2B or alpha-2C subtype. The human alpha-2-C10 clone (alpha-2A) and the rat RG20 clone have an 89% identity in their predicted amino acid sequence and are considered to be species orthologs. Although the expressed RG20 clone appears to have alpha-2D pharmacol., a careful comparison of its pharmacol. characteristics with the bovine pineal has not been reported previously. Based on the pKi values of a panel of 13 alpha-2 adrenergic agents that have been used previously to compare the alpha-2A, alpha-2B and alpha-2C subtypes, the pharmacol. characteristics of the bovine pineal alpha-2D receptor appear to be very similar to the rat RG20 clone (correlation coeff., r, of 0.93). The porcine ortholog of the human alpha-2-C10 receptor has pharmacol. characteristics identical to the human alpha-2A receptor (r = 0.99). Because of its higher affinity for the alpha-2D receptor, [3H]RX 821002 is a better radioligand than [3H]rauwolscine for studying this receptor subtype.
IT **67339-62-2**, ARC 239
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pharmacol. of .alpha.2A-adrenergic receptor of bovine and rat differ
from human and receptors)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 141 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



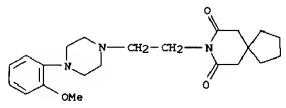
L14 ANSWER 142 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:225638 CAPLUS
DOCUMENT NUMBER: 122:1607
TITLE: Serotonin inhibition of adenylate cyclase in human platelet membranes; relation to 5-HT-1A receptor-mediated activity
AUTHOR(S): Newman, Michael E.
CORPORATE SOURCE: Dep. Psychiat., Hadassah Univ. Hosp., Jerusalem, Israel
SOURCE: Biochemical Pharmacology (1994), 48(9), 1677-82
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serotonin inhibited both basal and forskolin-stimulated adenylate cyclase activity in human platelet membranes by approx. 30%, with an EC50 of 54 nM. Addn. of NaCl to the assay medium reduced the degree of inhibition. 5-Carboxamidotryptamine (5-CT) behaved as a full agonist in this system (EC50 of 5.4 nM) and BMY 7378 and a partial agonist (inducing 19% inhibition); the putative 5-HT1A receptor agonists metergoline, spiroxatrine and MDL 73005 were inactive. The 5-HT1A receptor antagonists metitepin and NAN-190 behaved as antagonists with Kb or Ki values of 11.2 and 1.17 nM, resp. Spiperone behaved as a partial antagonist only. Epinephrine and 5-HT produced convergent, nonadditive inhibition of both basal and forskolin-stimulated cyclase.

IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin inhibition of adenylate cyclase in human platelet membranes in relation to serotoninergic S1A receptor)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

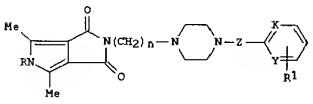


●2 HCl

L14 ANSWER 142 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:84779 CAPLUS
DOCUMENT NUMBER: 123:9354
TITLE: Synthesis and biological evaluation of derivatives of N-[4-substituted-1-piperazinylalkyl]-1-(butyl,aryl)-2,5-dimethylpyrrole-3,4-dicarboximide (Part II)
AUTHOR(S): Malinka, Wieslaw; Sieklucka-Dziuba, Maria; Robak, Jacek; Kleinrok, Zdzislaw
CORPORATE SOURCE: Dep. Drugs Chem., Medical Acad., Wroclaw, 50-137, Pol.
SOURCE: Farmaco (1994), 49(7-8), 481-7
CODEN: FRMCE8
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

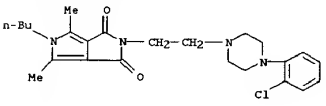


I

AB The title compds. I (n = 2-4; X, Y = CH, N; Z = -, CH2; R = Bu, Ph, 2-MeC6H4; R1 = H, Cl) have been prepd. by reaction of N-haloalkylimide derivs. with the corresponding N-monosubstituted piperazines. I were tested in preliminary pharmacol. investigations, and produced a general depressive action on the central nervous system.

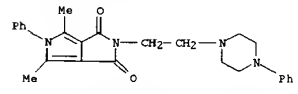
IT **159658-13-6P 159658-14-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and CNS activity of (piperazinylalkyl)pyrroledicarboximides)

RN 159658-13-6 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

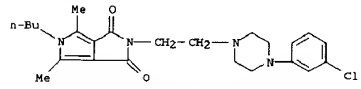


RN 159658-14-7 CAPLUS

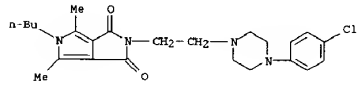
L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
4,6-dimethyl-5-phenyl-2-[2-(4-
phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT **159658-19-2P 159658-20-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and CNS activity of
(piperazinylalkyl)pyrroledicarboximides)
RN 159658-19-2 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
5-butyl-2-[2-[4-(3-chlorophenyl)-1-
piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

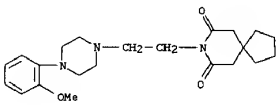


RN 159658-20-5 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
5-butyl-2-[2-[4-(4-chlorophenyl)-1-
piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:692532 CAPLUS
DOCUMENT NUMBER: 121:292532
TITLE: Effects of the putative 5-hydroxytryptamine1A antagonists BMY 7378, NAN 190 and (-)-propranolol on serotonergic dorsal raphe unit activity in behaving cats
AUTHOR(S): Fornal, Casimir A.; Marrosu, Franco; Metzler, Christine W.; Tada, Koji; Jacobs, Barry L.
CORPORATE SOURCE: Dep. Physiol., Princeton Univ., Princeton, NJ, USA
SOURCE: J. Pharmacol. Exp. Ther. (1994), 270(3), 1359-66
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent evidence from the authors lab. has demonstrated that blockade of somatodendritic 5-hydroxytryptamine (5-HT)1A autoreceptors by systemic administration of spiperone increases the firing rate of central serotonergic neurons in awake cats. The present study exams. the effects of 3 other putative 5-HT1A antagonists (BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]-decane-7,9-dione), NAN 190 (1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine) and (-)-propranolol) on the single-unit activity of serotonergic neurons recorded in the dorsal raphe nucleus of free-moving cats. Systemic administration of the phenylpiperazine derivs. BMY 7378 (5-100 .mu.g/kg i.v.) and NAN 190 (5-250 .mu.g/kg i.v.) produced a rapid, dose-dependent inhibition of neuronal activity with BMY 7378 being approx. twice as potent as NAN 190 (ED50 = 15.3 .mu.g/kg vs. 34.2 .mu.g/kg). The suppression of neuronal activity produced by both compds. was greatly attenuated by spiperone (1 mg/kg i.v.). Systemic administration of (-)-propranolol (2 and 4 mg/kg i.v.) produced a modest suppression of serotonergic neuronal activity which did not appear to be dose-related. The ability of BMY 7378, NAN 190 and (-)-propranolol to block the suppression of neuronal activity produced by 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT), a selective 5-HT1A agonist, was also examd. Pretreatment with these compds. had no significant effect on the inhibitory response of serotonergic neurons to 8-OH-DPAT challenge. These results indicate that BMY 7378 and NAN 190 act as agonists rather than antagonists at the somatodendritic 5-HT1A autoreceptor. Furthermore, (-)-propranolol, unlike spiperone, does not appear to be an effective 5-HT1A autoreceptor antagonist, because it did not block the action 8-OH-DPAT or increase basal serotonergic neuronal activity in awake animals.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of putative 5-hydroxytryptamine1A antagonists BMY 7378 and NAN

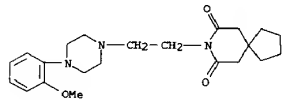
L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
190 and propranolol on serotonergic dorsal raphe unit activity in behaving cats)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:596576 CAPLUS
DOCUMENT NUMBER: 121:196576
TITLE: Serotonin and pain: Evidence that activation of 5-HT1A receptors does not elicit antinociception against noxious thermal, mechanical and chemical stimuli in mice
AUTHOR(S): Millan, Mark J.
CORPORATE SOURCE: Institut de Recherches Servier, Puteaux, 92800, Fr.
SOURCE: Pain (1994), 58(1), 45-61
CODEN: PAINDB; ISSN: 0304-3959
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, we examd. whether activation of 5-HT1A receptors elicits antinociception in response to acute noxious chem., thermal and mech. stimuli in mice. In the writhing test, both agonists (e.g., 8-OH-DPAT, S 14671 and WY 50,324) and partial agonists (e.g., buspirone and gepirone) elicited a pronounced antinociception. However, antagonists (e.g., (-)-alprenolol and WAY 100,135) also induced antinociception and, at lower (inactive) doses, failed to modify the action of agonists. In addn., the sepn. between doses required for induction of antinociception as compared to those required for induction of ataxia (in the rotarod test) was variable and low for both agonists (median: 1.9) and partial agonists (median: 1.3), although it was somewhat greater for antagonists (.gtoreq.3.3). In the hot-plate test, only certain agonists (e.g., 8-OH-DPAT) and partial agonists (e.g., gepirone) elicited antinociception and their actions were not attenuated by 5-HT1A antagonists which, themselves, were inactive in this paradigm. The 5-HT1C/2 antagonist, ritanserin, the 5-HT3 antagonist, ondansetron, the dopamine D2 receptor antagonist, raclopride, and the .alpha.1-adrenoceptor antagonist, prazosin, were also ineffective in modifying the antinociception evoked by 5-HT1A agonists and partial agonists in the hot-plate test. In contrast, their actions were strongly attenuated by the .alpha.2-adrenoceptor antagonist, idazoxan. In the tail-flick tests to noxious heat and noxious pressure, 5-HT1A receptor agonists, partial agonists and antagonists generally failed to induce antinociception. Moreover, modulation of stimulus intensity (from very weak to very intense) did not reveal any influence upon the latency to respond. In conclusion, in the writhing test, the data provide no evidence for a specific antinociceptive effect of the activation of 5-HT1A receptors. Further, in the hot-plate test, for those 5-HT1A agonists and partial agonists which induce

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
antinociception, .alpha.2-adrenoceptors rather than 5-HT1A receptors are
implicated in their actions. Finally, in reflexive tests, irresp. of stimulus quality or intensity, 5-HT1A agonists and partial agonists do not
mediate antinociception. These data suggest that the activation of 5-HT1A
receptors does not, under these conditions of acute noxious stimulation,
elicit antinociception.
IT **21102-95-4**, BMY 7378
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antinociception against noxious thermal, mech. and chem. stimuli in
mice)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1994:509676 CAPLUS
DOCUMENT NUMBER:	121:109676
TITLE:	Preparation of N-(2-oxoethyl)amino acid derivatives and peptides as immunosuppressants
INVENTOR(S):	Connell, Richard D.; Osterman, David D.; Katz, Michael E.
PATENT ASSIGNEE(S):	Miles Inc., USA
SOURCE:	Eur. Pat. Appl., 96 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

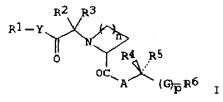
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 564924	A2	19931013	EP 1993-105035	19930326
EP 564924	A3	19931229		
EP 564924	B1	19980909		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2091194	AA	19931009	CA 1993-2091194	19930308
AT 170870	E	19980915	AT 1993-105035	19930326
ES 2119826	T3	19981016	ES 1993-105035	19930326
AU 9336773	A1	19931014	AU 1993-36773	19930406
AU 666179	B2	19960201		
JP 06041064	A2	19940215	JP 1993-106160	19930408
US 5686424	A	19971111	US 1995-431390	19950428

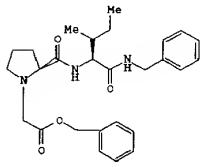
PRIORITY APPLN. INFO.: US 1992-864998 19920408
US 1992-981565 19921125

OTHER SOURCE(S): MARPAT 121:109676
GI

L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



I

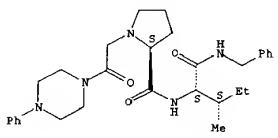


II

AB Title compds. I [R1 = H, (un)substituted alkyl, (un)substituted alkenyl,
cycloalkyl, etc.; Y = bond, O, (un)substituted imino; R1-Y = (un)substituted heterocyclyl; one of R2 and R3 = H and the other = alkyl;
n = 2, 3; A = O, (un)substituted imino; R4, R5 = H, (un)substituted alkyl,
etc.; G = CH:CH, CH2-CH2, CH2, NHCO; R6 = H, (un)substituted alkyl, (un)substituted Ph, etc.; p = 0, 1] are prepd. E.g., L-proline-L-isoleucine benzylamide (prepn. given) in MeCN was refluxed with benzyl
2-bromoacetate to give the title compd. II. In an in vitro study, this
had an IC50 of 2.2 .mu.M against peptidyl prolyl isomerase.
IT **156800-43-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as immunosuppressant)
RN 156800-43-0 CAPLUS
CN L-Isoleucinamide, 1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-L-prolyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS

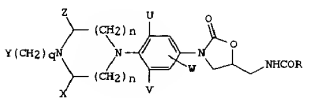
ACCESSION NUMBER: 1994:323599 CAPLUS
DOCUMENT NUMBER: 120:323599
TITLE: Oxazolidinones antibiotics containing a substituted diazine moiety
INVENTOR(S): Hutchinson, Douglas K.; Brickner, Steven Joseph; Barbachyn, Michael Robert; Gammill, Ronald B.; Patel, Mahest V.
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9323384	A1	19931125	WO 1993-US3570	19930421
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9342877	A1	19931213	AU 1993-42877	19930421
AU 668733	B2	19960516		
EP 640077	A1	19950301	EP 1993-912267	19930421
EP 640077	B1	20020626		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT				
JP 07506829	T2	19950727	JP 1993-520226	19930421
JP 3255920	B2	20020212		
HU 72296	A2	19960429	HU 1994-3208	19930421
CZ 281884	B6	19970312	CZ 1994-2505	19930421
RU 2105003	C1	19980220	RU 1994-46011	19930421
PL 174850	B1	19980930	PL 1993-321588	19930421
PL 174909	B1	19981030	PL 1993-306030	19930421
AT 219770	E	20020715	AT 1993-912267	19930421
ZA 9302855	A	19941024	ZA 1993-2855	19930422
IL 105555	A1	19980715	IL 1993-105555	19930429
CN 1079964	A	19931229	CN 1993-105039	19930508
CN 1044236	B	19990721		
NO 9404237	A	19950104	NO 1994-4237	19941107
FI 9405246	A	19941108	FI 1994-5246	19941108

PRIORITY APPLN. INFO.: US 1992-880432 A1 19920508
WO 1993-US3570 A 19930421

OTHER SOURCE(S): MARPAT 120:323599
GI

L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



I

AB The title compds. [I; R = H, (un)substituted C1-6 alkyl, C3-12 cycloalkyl, C1-6 alkoxy, etc.; U, V, W = (un)substituted C1-6 alkyl, F, Cl, Br, H; X, Z = C1-6 alkyl, C3-12 cycloalkyl, H; Y = H, C1-6 alkyl, aryl, OH, (un)substituted PhO, (un)substituted piperidino, etc.], effective against members of human and veterinary pathogens, including multiple-drug-resistant Staphylococci, Streptococci, anaerobic organisms such as Bacteroides and Clostridia, and acid-fast organisms such as Mycobacterium tuberculosis and Mycobacterium avium, are prepd. Thus, Me 4-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinecarboxylate, prepd. from 3,4-difluoronitrobenzene in 12 steps, demonstrated 50% oral ED in the Murine Assay procedure using female mice injected with S. aureus (UC# 6685) of 4.0 mg/kg, vs. 6.6 for ciprofloxacin.

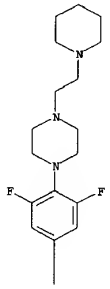
IT **154590-81-5 154590-90-6**
RL: RCT (Reactant)
(prepn. as antibiotic)

RN 154590-81-5 CAPLUS
CN Acetamide, N-[[3-[3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

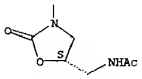
Absolute stereochemistry.

L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A



PAGE 2-A

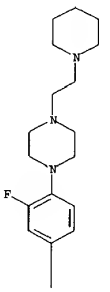


RN 154590-90-6 CAPLUS
CN Acetamide, N-[[3-[3-fluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)

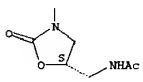
Absolute stereochemistry.

L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A

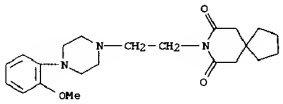


PAGE 2-A



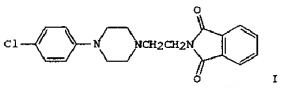
L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:316528 CAPLUS
DOCUMENT NUMBER: 120:316528
TITLE: Differential effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) on various 5-HT receptor binding sites in the rat brain
AUTHOR(S): Gozlan, H.; Laporte, A. M.; Thibault, S.; Schechter, L. E.; Bolanos, F.; Hamon, M.
CORPORATE SOURCE: INSERM U 288/Neurobiol. Cell. Fonctionnelle, Fac. Med. Pitie-Salpetriere, Paris, 75634, Fr.
SOURCE: Neuropharmacology (1994), 33(3-4), 423-31
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ), an alkylating agent producing irreversible blockade of various membrane bound receptors in brain, were investigated on four different types of serotonin receptors, 5-HT1A, 5-HT1B, 5-HT2A and 5-HT3, in various brain regions in the rat. In addn., the fate of central benzodiazepine- and R-zacopride-specific binding sites was also examd. in rats treated with EEOQ. Membrane binding assays and/or quant. autoradiog. with appropriate radioligands indicated that EEDQ inactivated 5-HT1A, 5-HT1B and 5-HT2A sites, but was poorly active on 5-HT3, benzodiazepine and "R" sites. Among the receptors affected by EEDQ, hippocampal 5-HT1A sites were the most sensitive to the alkylating agent (1D50.apprx.1 mg/kg i.p.), followed by the cortical 5-HT2A (ID50.apprx.6 mg/kg i.p.) sites. Pretreatment by selective ligands partially protected hippocampal 5-HT1A sites from irreversible inactivation by EEOQ (10 mg/kg i.p.) with the following order of efficacy: WAY 100135 > spiperone > BMY 7378 > ipsapirone. Similarly, pretreatment by spiperone (5 mg/kg i.p.) also reduced the ability of EEDQ to inactivate cortical 5-HT2A receptors. Analyses of the time-course recovery of resp. binding sites after EEDQ administration showed that the turnover rate of 5-HT1A sites did not significantly differ in the dorsal raphe nucleus and in various forebrain areas (hippocampus, septum, cerebral cortex; half-life .apprx.4 days), but was lower than that of cortical 5-HT2A sites (half-life: 2.9 days).
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotonin receptor binding by, receptor inactivation by EEOQ

L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
prevention by, in brain)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

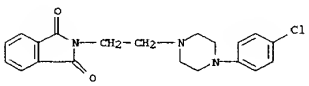
L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:261043 CAPLUS
DOCUMENT NUMBER: 120:261043
TITLE: Long lasting inhibition of food intake in the rat by a new phthalimidoethylpiperazine derivative
AUTHOR(S): Mustafa, A. A.; Al-Rashood, K. A.; El-Obeid, H. A.
CORPORATE SOURCE: Coll. Med., King Saud Univ., Riyadh, 11461, Saudi Arabia
SOURCE: Res. Commun. Psychol., Psychiatry Behav. (1993), 18(1-2), 25-36
CODEN: RCPBDC; ISSN: 0362-2428
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

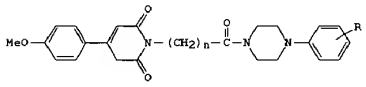
AB 1-[(P-Chlorophenyl)-4-(phthalimidoethyl)]piperazine (I; CPPEP), a newly synthesized compd., produced a dose-dependent inhibition of food intake in food-deprived male Wistar rats. This effect was still apparent three days after injection of the compd. The anorectic effect was not antagonized by either the non-selective 5-HT receptor antagonist, methylsergide (5 mg kg-1, i.p.), nor by the 5-HT2 receptor antagonist, ketanserin (1 mg kg-1, i.p.), pindolol (4 mg kg-1, i.p.), which blocks .beta.-adrenoceptors and some of the effects mediated at 5-HT1 receptors, did not block the redn. in food intake produced by the compd. Similarly the non-selective alpha-adrenoceptor antagonist, phentolamine (5 mg kg-1, i.p.) and the .alpha.2-adrenoceptor blocker, yohimbine (2 mg kg-1, i.p.) did not affect the anorectic effect of CPPEP. The hypophagic effect of CPPEP, however, was antagonized by the D2-dopamine receptor blocker, (.+-.) sulpiride (30 mg kg-1, i.p.) and by the relatively selective 5-HT3 receptor antagonist, zacopride (1 mg kg-1, i.p.). None of the antagonists used had any effect on food intake when they were administered alone. It is concluded that

L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
the anorectic action of CPPEP is mediated, at least in part, by interaction with 5-HT3 receptors.
IT **75000-30-5**
RL: PRP (Properties)
(long-lasting anorectic effect of, serotoninergic S3 receptors in)
RN 75000-30-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

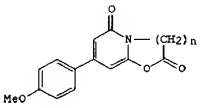


L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:244969 CAPLUS
DOCUMENT NUMBER: 120:244969
TITLE: Synthesis of 1-arylpiperazine amides of 2-[4-(methoxyphenyl)-1H,5H-pyridin-2,6-dione-1-yl]acetic, -propionic acids
AUTHOR(S): Thakur, K. D.; Samant, S. D.
CORPORATE SOURCE: Org. Chem. Res. Lab., Univ. Dep. Chem. Technol., Bombay, 400 019, India
SOURCE: J. Indian Chem. Soc. (1993), 70(3), 261-3
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:244969
GI



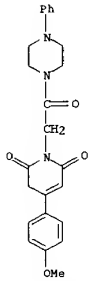
I



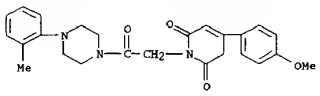
II

AB The title compds. I (R = H, 2-, 3-, 4-Me, 3-, 4-Cl, n = 1, 2) were prepd.
by condensing oxazolo/oxazinopyridinediones II with the corresponding arylpiperazine.
IT **154147-05-4P 154147-06-5P 154147-07-6P**
154147-08-7P 154147-09-8P 154147-10-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 154147-05-4 CAPLUS
CN Piperazine, 1-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

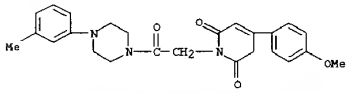
L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 154147-06-5 CAPLUS
CN Piperazine, 1-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

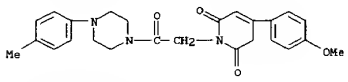


RN 154147-07-6 CAPLUS
CN Piperazine, 1-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]-4-(3-methylphenyl)- (9CI) (CA INDEX NAME)

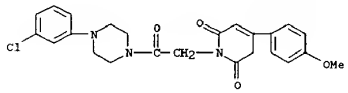


RN 154147-08-7 CAPLUS
CN Piperazine, 1-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)

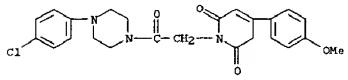
L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 154147-09-8 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]- (9CI) (CA INDEX NAME)



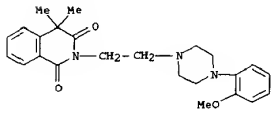
RN 154147-10-1 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-pyridinyl]acetyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 151 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:182875 CAPLUS
DOCUMENT NUMBER: 120:182875
TITLE: Further characterization of human .alpha.2-adrenoceptor subtypes: [3H]RX821002 binding and definition of additional selective drugs
AUTHOR(S): Devedjian, Jean Christophe; Esclapez, Francoise; Denis-Pouxviel, Colette; Paris, Herve
CORPORATE SOURCE: Inst. Louis Bugnard, CHU Rangueil, Toulouse, 31054, Fr.
SOURCE: Eur. J. Pharmacol. (1994), 252(1), 43-9
CODEN: EJPHA2; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The characteristics of [3H]RX821002 binding to the different human .alpha.2-adrenoceptor subtypes were studied on membranes from COS-7 cells transfected with the genes: .alpha.2C2, .alpha.2C4 and .alpha.2C10. Satn. expts. indicated that the radioligand labels the three adrenoceptors with high affinity. A difference was however obsd. between the subtypes. The affinity of [3H]RX821002 for .alpha.2C10-adrenoceptors (KD = 1.41 .+-. 0.15 nM) was 3-fold higher than for .alpha.2C4-adrenoceptors (KD = 4.42 .+-. 0.63 nM) and 7-fold higher than for .alpha.2C2-adrenoceptors (KD = 10.2 .+-. 0.9 nM). Inhibition expts. with a series of 17 competitors confirmed that prazosin, oxymetazoline, WB4101, ARC239, corynanthine and chlorpromazine are subtype-selective drugs. They also demonstrated that BRL44408 and guanfacine are selective for the .alpha.2C10-receptor, whereas BRL41992 and imiloxan are selective for the .alpha.2C2. Given that these two latter drugs were previously shown to be specific for the .alpha.2B pharmacol. subtype originally defined in neonatal rat lung, these results confirm that the .alpha.2C2 gene encodes for the human homolog of this receptor subtype. It is concluded that the combined use of [3H]RX821002 and of these new selective drugs may be useful for the identification of the .alpha.2-adrenoceptor subtypes in human tissues.
IT **67339-62-2**, ARC239
RL: BIOL (Biological study)
(.alpha.2-adrenoceptor subtypes binding of, in human cell membranes)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 151 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS

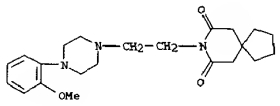
ACCESSION NUMBER: 1994:96856 CAPLUS
DOCUMENT NUMBER: 120:96856
TITLE: Electrophysiological evidence for a large receptor reserve for inhibition of dorsal raphe neuronal firing by 5-HT1A agonists
AUTHOR(S): Cox, Richard F.; Meller, Emanuel; Waszczak, Barbara L.
CORPORATE SOURCE: Bouve Coll. Pharm. Health Sci., Northeast. Univ., Boston, MA, 02115, USA
SOURCE: Synapse (N. Y.) (1993), 14(4), 297-304
CODEN: SYNAET; ISSN: 0887-4476
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies (Meller et al. 1990) have shown that a large receptor reserve exists for the inhibition of 5-HT synthesis in rat cortex and hippocampus by the 5-HT1A agonist 8-hydroxy-2(di-n-propylamino)tetralin (8-OH-DPAT), whereas little or no reserve exists for the lower efficacy agonists ipsapirone and BMY 7378. The current studies were undertaken to det. if the above drugs exhibit similar relative efficacies and receptor reserves in an electrophysiol. model of 5-HT1A receptor activation, i.e., the inhibition of dorsal raphe cell firing. I.v. dose-response curves were constructed in untreated control rats, or in rats which received an injection of the irreversible receptor inactivator N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ, 6 mg/kg, s.c.) 24 h before recording. All 3 drugs fully inhibited dorsal raphe cell firing in control rats (ED50's: 1.5 .mu.g/kg, 8-OH-DPAT; 30.0 .mu.g/kg, ipsapirone; 17.5 .mu.g/kg, BMY 7378). However, unlike effects on 5-HT synthesis, EEDQ treatments caused no depression of the maximal inhibitory response for any of the agonists, although all dose-response curves were shifted to the right (ED50's: 10.1 .mu.g/kg, 6.7-fold shift, 8-OH-DPAT; 139.9 .mu.g/kg, 4.7-fold shift, ipsapirone; 53.8 .mu.g/kg, 3.1-fold shift, BMY 7378). Although the order of agonist efficacies was similar for both inhibition of 5-HT synthesis and dorsal raphe cell firing (8-OH-DPAT > ipsapirone > BMY 7378), a large (>50%) receptor reserve was estd. for all 3 drugs in this electrophysiol. system. This suggests that 5-HT1A receptor populations mediating the inhibition of transmitter synthesis and neuronal firing may be differently regulated or have different receptor-effector coupling characteristics (G-proteins, effectors, and/or transduction efficiencies).

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)

L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(dorsal raphe neuron firing inhibition by, receptor reserve for serotonin formation inhibition and)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:95766 CAPLUS
DOCUMENT NUMBER: 120:95766
TITLE: Preparation containing interferon-.alpha. and histamine, serotonin or substances with corresponding receptor activity for activation of natural killer cells
INVENTOR(S): Hellstrand, Kristoffer; Hermodsson, Svante
PATENT ASSIGNEE(S): Estero-Anstalt, Liechtenstein
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324144	A1	19931209	WO 1993-SE496	19930603
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9201719	A	19931204	SE 1992-1719	19920603
SE 513429	C2	20000911		
AU 9343660	A1	19931230	AU 1993-43660	19930603
AU 672610	B2	19961010		
EP 652768	A1	19950517	EP 1993-913731	19930603
EP 652768	B1	20000503		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502024	T2	19960305	JP 1993-500471	19930603
JP 2888259	B2	19990510		
ES 2147758	T3	20001001	ES 1993-913731	19930603
US 5728378	A	19980317	US 1995-374787	19950508

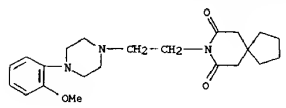
PRIORITY APPLN. INFO.: SE 1992-1719 A 19920603
WO 1993-SE496 A 19930603

AB Pharmaceutical prepns. for activation of natural killer cells, for example in order to treat tumors or virus infections, comprises a first compn. contg. interferon-.alpha. or analogs thereof, together with a second compn. contg. at least one substance with H2 or 5-HT1a receptor agonist activity, for example, histamine or serotonin. The first and second compns. are either mixed in a prepn. or furnished in sep. doses. A combination of interferon-.alpha. and histamine showed a synergistic antitumor activity of natural killer cells against cultured target cells.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(natural killer cell activation by .alpha.-interferon and)

RN 21102-95-4 CAPLUS

L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

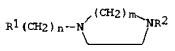


●2 HCl

L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:77181 CAPLUS
DOCUMENT NUMBER: 120:77181
TITLE: Preparation of hexahydroazepine derivatives as 5-HT1A serotoninergic receptor antagonists
INVENTOR(S): Takahashi, Nobuyuki; Suzuki, Yukio; Mochizuki, Daisuke; Tsujita, Ryuichi; Yaso, Masao; Komaki, Hisayuki
PATENT ASSIGNEE(S): Asahi Kasei Kogyo K. K., Japan
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311116	A1	19930610	WO 1992-JP1533	19921124
W: CA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 05345764	A2	19931227	JP 1992-307377	19921117
PRIORITY APPLN. INFO.:			JP 1991-336053	19911126
			JP 1992-307377	19921117

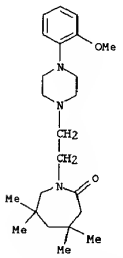
OTHER SOURCE(S): CASREACT 120:77181; MARPAT 120:77181
GI



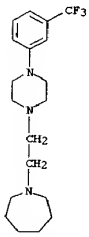
I

AB The title compds. [I; R1 = (un)substituted hexahydroazepin-1-yl; R2 = (un)substituted Ph, e.g., (trifluoromethyl)phenyl, (un)substituted pyridazinyl or 1,2-benzisothiazolyl; n = 2-5 integer; m = 2, 3], 5-HT1A serotoninergic receptors and therefore useful for treatment of many ailments, e.g., anxiety, depression, motion sickness, hypertension (no data), are prepd. E.g., caprolactam was treated with Cl-(CH2)3-Br in THF contg. NaH at room temp. for 5 h to give 1-(3-chloropropyl)hexahydro-1H-azepine, which was refluxed with 1-[3-(trifluoromethyl)phenyl]piperazine in benzene contg. Et3N for 139 h to give I [R1 = hexahydro-1H-azepin-1-yl, R2 = 3-(trifluoromethyl)phenyl, n = 3, m = 2], which had an affinity (Ki) of 13.7 nM for 5-HT1A receptors.
IT **151142-17-5P 151142-46-0P 151142-47-1P 151142-48-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic receptor antagonist)
RN 151142-17-5 CAPLUS

L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 2H-Azepin-2-one, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4,6,6-tetramethyl- (9CI) (CA INDEX NAME)

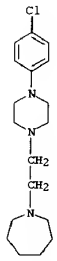


RN 151142-46-0 CAPLUS
CN 1H-Azepine, hexahydro-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

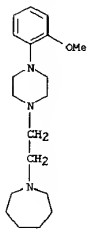


RN 151142-47-1 CAPLUS
CN 1H-Azepine, 1-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]hexahydro- (9CI) (CA INDEX NAME)

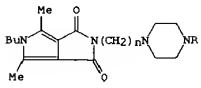
L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 151142-48-2 CAPLUS
CN 1H-Azepine, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 155 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:45179 CAPLUS
DOCUMENT NUMBER: 120:45179
TITLE: Synthesis and pharmacological properties of N-(4-substituted-1-piperazinylalkyl)-1-butyl-2,5-dimethylpyrrole-3,4-dicarboxyimide derivatives
AUTHOR(S): Malinka, Wieslaw; Tatarczynska, Ewa
CORPORATE SOURCE: Dep. Pharm., Med. Acad. Wroclaw, Wroclaw, 51-137, Pol.
SOURCE: Farmaco (1993), 48(7), 933-47
CODEN: FRMCE8
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

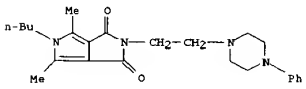


I

AB The prepn. of a no. of title compds. (I; R = ph, Me, pyridinyl, pyrimidinyl) is described. The structures of the novel compds. were confirmed by elemental and spectral analyses. The results of a preliminary pharmacol. study of CNS effects caused by I are presented.

IT **151722-70-2P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(prepn. and pharmacol. of, structure in relation to)

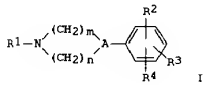
RN 151722-70-2 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-4,6-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:8615 CAPLUS
DOCUMENT NUMBER: 120:8615
TITLE: Phenyl-substituted heterocyclic antiviral agents
INVENTOR(S): Kurono, Masayasu; Baba, Yutaka; Iwata, Noriyuki; Kakigami, Takuji; Isogawa, Kogaku; Mitani, Takahiko; Ishiwata, Yoshiro; Yokochi, Shoji; Otsuka, Tamaki; et al.
PATENT ASSIGNEE(S): Sanwa Kagaku Kenkyusho Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 548798	A1	19930630	EP 1992-121466	19921217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 05255089	A2	19931005	JP 1992-343127	19921130

PRIORITY APPLN. INFO.: JP 1991-335028 19911218
OTHER SOURCE(S): MARPAT 120:8615
GI



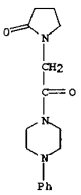
I

AB The title compds. I [A = N, CH2; R1 = alkyl, acyl, arylsulfonyl, alkylsulfonyl, Ph, heterocyclic; R2-R4 = H, NH2, alkylamino, acylamino, alkyl, HO, alkyloxy, halogen, CO2H, NO2, cyano, SH, etc.; m = 0, natural no.; n = natural no.], useful against infectious diseases caused by DNA viruses, RNA viruses, or retroviruses, are prepd. Thus, 1-(2-chlorophenyl)piperazine was condensed with Me 2-pyrrolidone-1-acetate, producing 1-(2-chlorophenyl)-4-(2-pyrrolidon-1-ylacetyl)piperazine (II) in 77.1% yield. II demonstrated no tissue cytotoxicity and had antiviral activity against herpes simplex virus type 1 at 10 .mu.g/mL.

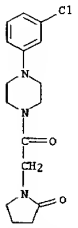
IT **131027-95-7 131028-02-9 135459-98-2 150558-40-0 150558-41-1 150558-42-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antiviral activity of)

RN 131027-95-7 CAPLUS

L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

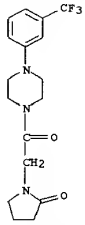


RN 131028-02-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

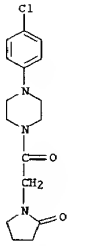


RN 135459-98-2 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

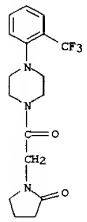
L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



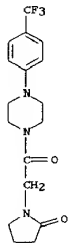
RN 150558-40-0 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)



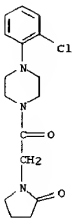
RN 150558-41-1 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 150558-42-2 CAPLUS
CN Piperazine,
1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[4-(trifluoromethyl)phenyl]-
(9CI) (CA INDEX NAME)

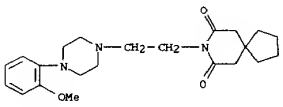


IT **150557-71-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of)
RN 150557-71-4 CAPLUS
CN Piperazine, 1-(2-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-
(9CI)
(CA INDEX NAME)



ACCESSION NUMBER: 1993:531752 CAPLUS
DOCUMENT NUMBER: 119:131752
TITLE: Identification of residues important for ligand binding to the human 5-hydroxytryptaminelA serotonin receptor
AUTHOR(S): Chanda, Pranab K.; Minchin, Michael C. W.; Davis, Alan R.; Greenberg, Lynda; Reilly, Yvonne; McGregor, William H.; Bhat, Ramesh; Lubeck, Michael D.; Hung, Paul P.
CORPORATE SOURCE: Dep. Biotechnol. Microbiol., Wyeth-Ayerst Res., Philadelphia, PA, 19101, USA
SOURCE: Mol. Pharmacol. (1993), 43(4), 516-20
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The functional significance of the conserved amino acids within transmembrane regions II and VII of the human 5-hydroxytryptamine (5-HT)1A receptor was analyzed by oligonucleotide-directed mutagenesis followed by transient expression of the mutated receptor genes in COS-1 cells. The substitution of a conserved asparagine at position 396 (transmembrane region VII) with either alanine, phenylalanine, or valine resulted in a receptor that did not bind the 5-HT1A agonist 8-hydroxy-2-(di-n-[3H]propylamino)tetralin. In contrast, replacement of Asn396 with glutamine did not affect agonist binding. In addn., serine residues at positions 391 and 393 (transmembrane domain VII) were changed to alanine. Changing the less conserved Ser391 to alanine had no effect on ligand binding. However, replacement of the conserved Ser393 with alanine reduced ligand binding by 86%. Replacement of a conserved aspartate at position 82 (transmembrane region II) with alanine also produced a receptor without detectable agonist binding. Protein immunoblotting detected receptor protein of approx. 51 kDa in both wild-type and mutant receptor-expressing cells, indicating that these mutations probably did not affect expression or processing of the protein. Importantly, the sequence of the human 5-HT1A receptor described in this paper differs from the published sequence in transmembrane region IV. The present sequence encodes a protein of 422 amino acids, instead of the 421-amino acid protein that has been described previously and has a change in the sequence in transmembrane region IV from...RPRAL... to...RRAAA..., which corresponds to the published sequence of the rat 5-HT1A receptor. Moreover, conversion of the transmembrane region IV sequence of the present clone to that of the published sequence by site-directed

mutagenesis abolished ligand binding to the receptor.
IT **21102-95-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); BIOL (Biological study)
(5-HT1A receptor of human binding by, site for)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

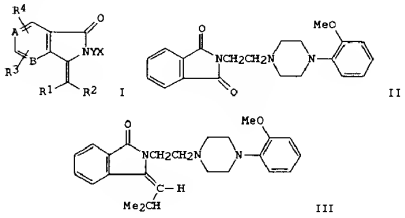


●2 HCl

L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:495325 CAPLUS
DOCUMENT NUMBER: 119:95325
TITLE: Preparation of 3-methyleneisoindolin-1-one derivatives for treating ischemic cerebral disorders
INVENTOR(S): Mohri, Shinichiro; Obase, Hiroyuki; Ikeda, Junichi; Kubo, Kazuhiro; Mori, Akihisa; Ishii, Akio
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217448	A1	19921015	WO 1992-JP246	19920302
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
PRIORITY APPLN. INFO.:			JP 1991-68379	19910401
OTHER SOURCE(S):		MARPAT 119:95325		

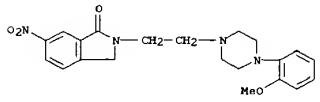
GI



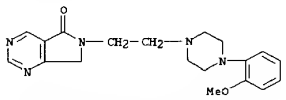
AB The title compds. [I; A, B = CH, N; R1, R2 = alkyl; R3, R4 = halo, alkoxy, etc.; X = (substituted) heterocyclyl; Y = (CH2)1-4] are prepd. A soln. of Me2CHCH2MgBr in THF was added to a soln. of imide II in THF with stirring at room temp. under Ar, 4 N HCl was added with stirring, followed by H2O and 10 N NaOH, and the mixt. was extd. with EtOAc to give 50% III, which as a phosphate salt showed min. ED of 6.3 mg/kg p.o. for cerebral protection in mice.

IT **149263-56-9P 149263-60-5P 149263-65-0P 149263-66-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of ischemic cerebral disease drug)

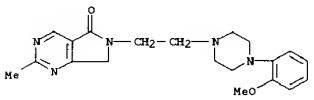
RN 149263-56-9 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro- (9CI) (CA INDEX NAME)



RN 149263-60-5 CAPLUS
CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

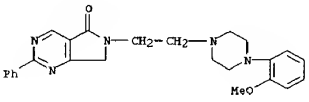


RN 149263-65-0 CAPLUS
CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



RN 149263-66-1 CAPLUS
CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-phenyl- (9CI) (CA INDEX NAME)

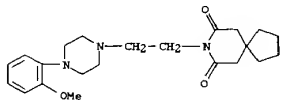
L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:421024 CAPLUS
DOCUMENT NUMBER: 119:21024
TITLE: Studies of the biochemical basis for the discriminative properties of 8-hydroxy-2-(di-n-propylamino)tetralin
AUTHOR(S): Rabin, Richard A.; Winter, J. C.
CORPORATE SOURCE: Dep. Pharmacol., State Univ. New York, Buffalo, NY, 14214, USA
SOURCE: Eur. J. Pharmacol. (1993), 235(2-3), 237-43
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of a series of compds. to mimic the stimulus properties of 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) was compared to: the affinity of these compds. for the 5-HT1A receptor; and their efficacy to inhibit forskolin-stimulated adenylate cyclase activity. Although for 9 compds. (flexinoxan, MDL 73005EF, gepirone, ipsapirone, buspirone, tandospirone, yohimbine, L 657,743 and rauwolscine) complete cross generalization was assocd. with high affinity for the 5-HT1A receptor, eltoprazine, LSD and BMY 7378 had pKD > 7.44, but did not show complete mimicry of 8-OH-DPAT. In addn., indorenate had a pKD of 7.88, yet the behavioral response was indistinguishable from the saline control. Because the above data indicated that affinity for the 5-HT1A receptor was necessary, but not sufficient for a receptor ligand to mimic 8-OH-DPAT, the in vitro efficacy of the various compds. at the 5-HT1A receptor was detd. by measuring inhibition of forskolin-stimulated adenylate cyclase activity in hippocampal membranes. For a series of drugs (gepirone, ipsapirone, flesinoxan, buspirone, tandospirone, yohimbine, L 657,743 and rauwolscine) inhibition of forskolin-stimulated adenylate cyclase activity was obsd., and these same drugs showed complete cross generalization. However, BMY 14802 and MDL 73005EF did not alter adenylate cyclase activity, yet completely mimicked the stimulus properties of 8-OH-DPAT. Eltoprazine showed efficacy in inhibiting forskolin-stimulated adenylate cyclase activity, but only 30% of the responses following administration of this drug were on the 8-OH-DPAT-appropriate lever. Furthermore, although indorenate inhibited hippocampal adenylate cyclase activity, the behavioral response to this compd. was indistinguishable from the saline control. The present study indicates that activation of the 5-HT1A receptor neg. coupled to adenylate cyclase is neither necessary nor sufficient for a receptor ligand to mimic the stimulus properties of

L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
8-OH-DPAT.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotonin S1A receptor affinity of, hydroxy(dipropylamino)tetralin action in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

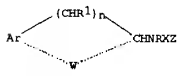


●2 HCl

L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:225698 CAPLUS
DOCUMENT NUMBER: 118:225698
TITLE: Preparation of .sigma. receptor ligands as drugs for treratment of central nervous system disorders
INVENTOR(S): Glennon, Richard A.
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9300313	A2	19930107	WO 1992-US5330	19920626
WO 9300313	A3	19930304		
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 6057371	A	20000502	US 1992-894771	19920610
CA 2111957	AA	19930107	CA 1992-2111957	19920626
AU 9222945	A1	19930125	AU 1992-22945	19920626
AU 676993	B2	19970410		
ZA 9204775	A	19930416	ZA 1992-4775	19920626
EP 591426	A1	19940413	EP 1992-914789	19920626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06509069	T2	19941013	JP 1992-501248	19920626

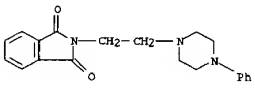
PRIORITY APPLN. INFO.: US 1991-720173 19910627
US 1992-894771 19920610
WO 1992-US5330 19920626
OTHER SOURCE(S): MARPAT 118:225698
GI



I

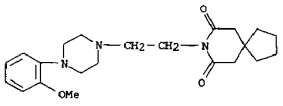
AB The phenylalkylamines, aminotetralins, piperazines, and piperidines I [Ar = (un)substituted aryl or heteroaryl; R = H, alkyl; R1 = R, alkoxy, chloro, etc.; RR1 = morpholino, piperazinyl, piperidinyl; W = (CH2)p, -H H-; X = (CH2)q, (CH2)rC.tplbond.(CH2)r, etc.; Z = H, cycloalkyl,aryl, etc.; n = 0-5; p = 1-3; q = 1-6; r = 0-3] are prepd. as selective .sigma.-receptor-binding agents, useful for the treatment of gastroenteral

L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and central nervous system disorders and drug abuse. Since I do not bind to dopaminergic, PCP and 5-HT1A receptors, they are free of the side effects of the conventional neuroleptic agents. The reaction of R-(-)-amphetamine with 2-phenoxyethyl chloride, at 95.degree., gave R-(-)-N-(2-phenoxyethyl)-1-phenyl-2-aminopropane-HCl. The .sigma.-, PCP-, and dopamine-receptor binding assays were carried out by the method of Weber et al. (1986), using guinea pig brain membrane homogenates and the radioligand [3H]di-o-tolylguanidine.
IT **75000-24-7**
RL: BIOL (Biological study)
(central nervous and gastrointestinal agent, as sigma receptor ligand)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
(CA INDEX NAME)



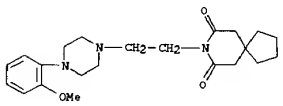
L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:94851 CAPLUS
DOCUMENT NUMBER: 118:94851
TITLE: Allosteric interactions between the binding sites of receptor agonists and guanine nucleotides: A comparative study of the 5-hydroxytryptamine1A and adenosine A1 receptor systems in rat hippocampal membranes
AUTHOR(S): Mahle, Cathy D.; Wiener, Harvey L.; Yocca, Frank D.; Maayani, Saul
CORPORATE SOURCE: Mount Sinai Sch. Med., City Univ. New York, New York, NY, USA
SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(3), 1275-84
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ternary complex formed between agonist, receptor, and guanine nucleotide-binding protein and its destabilization by guanine nucleotides (GN) were utilized to study early events in signal transduction, by characterizing the allosteric interactions between agonist and GN binding to the receptor/guanine nucleotide-binding protein, G complex for adenosine A1 and 5-HT1A receptors. The functional interaction between the ternary complex and GTP was examd. by assaying adenylyl cyclase activity.
Binding of a full adenosine A1 agonist ([3H]-R-(-)-N6-(2-phenylisopropyl)adenosine} and a full {(.+-.)-[3H]-8-hydroxydipropylaminotetralin} ([3H]I) and partial {[3H]-8-[2-[4-(2-methoxypheny1)-1-piperazinyl]ethyl]-8-azaspiro1[4.5]-decane-7,9-dione} ([3H]I1) 5-HT1A agonist was examd. in relation to the binding of GN. The amt. of ternary complex formed depended upon receptor type and drug relative efficacy. The ratio between the drug's EC50 value (adenylyl cyclase) and dissocn. const. (Kd) was also receptor and drug relative efficacy dependent. 5'-Guanylylimidodiphosphate (100 .mu.M) caused an .apprx.50% decrease in the Bmax for all drugs without affecting Kd values.
5'-Guanylylimidodiphosphate and guanosine 5'-O-(3-thiotriphosphate) attenuated [3H]-agonist binding in a concn.-dependent and saturable manner, with IC50 values increased 2-6-fold with increasing receptor occupancy. IC50 values were approx. one-tenth lower at the 5-HT1A receptor than at tje adenosine A1 receptor; similar values were obtained for inhibition of [3H]I and [3H]I1 binding, suggesting an independence of agonist efficacy. It is proposed that the stabilization of the ternary complex by hormone binding, measured by Bmax values, is related to drug-relative efficacy; thus, the amt. of ternary complex available for destabilization by GN is greater for the more efficacious agonist. This

L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
is translated into greater relative efficacy obsd. in the maximal inhibition of adenylyl cyclase.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotoninergic S1A receptor binding of, in hippocampus, allosteric
interactions between binding sites of receptor agonist and guanine nucleotides in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

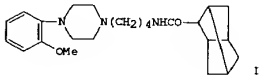
L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

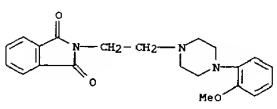
L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:32850 CAPLUS
DOCUMENT NUMBER: 118:32850
TITLE: Yohimbine as a serotonergic agent: evidence from receptor binding and drug discrimination
AUTHOR(S): Winter, J. C.; Rabin, Richard A.
CORPORATE SOURCE: Sch. Med. Biomed. Sci., State Univ. New York, Buffalo, NY, USA
SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(2), 682-9
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stimulus control was established in rats trained to discriminate either 8-hydroxy-2-(di-n-propylamino)tetralin (DPAT) (0.2 mg/kg or yohimbine (3 mg/kg) from saline. Tests of generalization were then conducted with a group of drugs thought to act via the 5-hydroxytryptaminelA (5-HT1A) receptor and a group to drugs thought to act as antagonists at .alpha.2-adrenoceptors. In addn., each drug was characterized in terms of its affinity for 5-HT1A and .alpha.2- adrenoceptors by means of radioligand binding techniques. It was obsd. that the stimulus effects of DPAT generalized fully to those of the .alpha.2-adrenoceptor antagonists, yohimbine, rauwolscine and L-657,743, but not to idazoxan or atipamezole. The dissocn. consts. (Kd, nM) of the .alpha.2-adrenoceptor antagonists at the 5-HT1A receptor were 74, 52, 80, 199 and 13,000, resp. Thus, the discrimination data are explicable in terms of a direct action of yohimbine and some other .alpha.2-adrenoceptor antagonist upon 5-HT1A receptors. In yohimbine-trained rats, full generalization to DPAT, flesinoxan and tandospirone was obsd. In light of the negligible affinity of flesinoxan and tandospirone for the .alpha.2-adrenoceptor (9000 and 8800 nM, resp.), and high affinity for the 5-HT1A receptor (0.3 and 43 nM, resp.), a mechanism mediated by the latter site is suggested. The present data suggest that rats trained with yohimbine as a discriminative stimulus generalize to drugs with minimal affinity for the .alpha.2-adrenoceptor but with high affinity for 5-HT1A receptors. Studies in which yohimbine is used to assess the function of the .alpha.2-adrenoceptor should also consider the possible involvement of 5-HT1A receptors.
IT **21102-95-4**, BMY7378
RL: BIOL (Biological study)
(yohimbine binding to serotonergic S1A and .alpha.2-adrenergic receptors response to)
RN 21102-95-4 CAPLUS

L14 ANSWER 163 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:626102 CAPLUS
DOCUMENT NUMBER: 117:226102
TITLE: 4-[4-(1-Noradamantanecarboxamido)butyl]-1-(2-methoxyphenyl)piperazine: a high-affinity 5-HT1A-selective agent
AUTHOR(S): El-Bermawy, Mohamed; Raghupathi, Reva; Ingher, Stacy P.; Teitler, Milt; Maayani, Saul; Glennon, Richard A.
CORPORATE SOURCE: Dep. Med. Chem., Med. Coll. Virginia, Richmond, VA, 23298, USA
SOURCE: Med. Chem. Res. (1992), 2(2), 88-95
CODEN: MCREEB; ISSN: 1054-2523
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



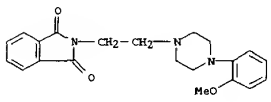
I

AB A problem with many arylpiperazine 5-HT1A ligands is their high affinity for .alpha.1-adrenergic, D2 dopamine, and/or 5-HT2 serotonin receptors. The title compd. (I) binds with very high affinity at 5-HT1A receptors (Ki = 0.1 nM) and with 460- 260- and 400-fold selectivity over .alpha.1-adrenergic, D2, and 5-HT2 receptors, resp. Preliminary studies indicate that I is a 5-HT1A partial agonist (intrinsic activity = 0.4) with 140-fold the affinity of the std. agent buspirone.
IT **99718-67-9P 144391-85-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as high affinity 5-HT1A-selective agent)
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 163 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 144391-85-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
, monohydrochloride (9CI) (CA INDEX NAME)



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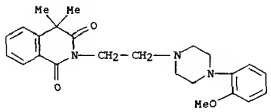
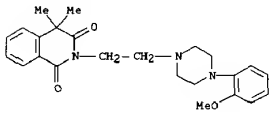
L14 ANSWER 164 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 164 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:605626 CAPLUS
DOCUMENT NUMBER: 117:205626
TITLE: The .alpha.2-adrenoceptors of the human retinoblastoma cell line (Y79) may represent an additional example of the .alpha.2C-adrenoceptor
AUTHOR(S): Gleason, Marie M.; Mieble, J. Paul
CORPORATE SOURCE: Dep. Pharmacol., SmithKline Beecham Pharm., King of Prussia, PA, 19406, USA
SOURCE: Br. J. Pharmacol. (1992), 107(1), 222-5
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In agreement with the literature, correlation of the ability of a series of agonists and antagonists to displace [3H]rauwolscine binding shows the .alpha.2-adrenoceptors of HT29 cells, NG108-15 cells, OK cells, and homogenates of rat sublingual gland to represent 4 distinct subtypes. [3H]rauwolscine also bound with high affinity (KD = 0.30 nM) to a human retinoblastoma cell line (Y79). Specific binding represents 73% of total binding, and a Bmax of 38 fmol/mg protein was detd. Correlation of antagonist affinities against [3H]rauwolscine with corresponding values in the other 4 tissue sources showed the Y79 cells to resemble most closely the OK cells, the prototype example of an .alpha.2C-adrenoceptor, with a correlation coeff. of 0.90 and a regression slope of 1.01 being obtained for 10 antagonists in these two systems. Comparison of KD values for [3H]rauwolscine also showed a similarity between the OK cells (0.19 nM) and Y79 cells. These data suggest that the human retinoblastoma cell line may represent an addnl. example of the .alpha.2C-adrenoceptor subtype.
IT **67339-62-2**, ARC 239
RL: BIOL (Biological study)
(rauwolscine binding by various .alpha.2-adrenoceptor subtypes inhibition by)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

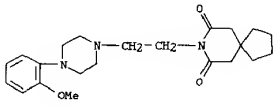
L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:543163 CAPLUS
DOCUMENT NUMBER: 117:143163
TITLE: .alpha.2 Adrenoceptor and catecholamine-insensitive binding sites for [3H]rilmenidine in membranes from rat cerebral cortex
AUTHOR(S): King, Paul R.; Gundlach, Andrew L.; Jarrott, Bevyn; Louis, William J.
CORPORATE SOURCE: Clin. Pharmacol. Ther. Unit, Austin Hosp., Heidelberg, 3084, Australia
SOURCE: Eur. J. Pharmacol. (1992), 218(1), 101-8
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetic and pharmacol. characteristics of the binding of the oxazoline antihypertensive drug, [3H]rilmenidine, to membranes of rat cerebral cortex have been detd. Computerized resoln. of curvilinear, equil. binding isotherms was consistent with the existence of two distinct binding sites for [3H]rilmenidine: Kd 17.3 .+-. 7.41 nM, Bmax 0.197 .+-. 0.06 pmol/mg protein and Kd 254 .+-. 48 nM, Bmax 1.59 .+-. 0.08 pmol/mg protein. Moreover, the resoln. of two assocn. and dissocn. rates also suggested the existence of two binding site populations. Drug inhibition studies revealed that specific binding of [3H]rilmenidine (2 nM) was only inhibited by a max. of 50% by the catecholamines, adrenaline and noradrenaline, but was completely inhibited by some oxazolines, by guanabenz (a guanidino drug) and by several imidazoline compds. including naphazoline, oxymetazoline and clonidine. Binding isotherms for these drugs were also best fit by a two-site model. The relative Ki values at the high affinity site for [3H]rilmenidine and the no. of these high affinity sites are consistent with this site being an .alpha.2-adrenoceptor. The high affinity of oxymetazoline and low affinity of prazosin for high affinity [3H]rilmenidine binding sites together with the rank order of potency of oxymetazoline > phentolamine > SKF 104078 > ARC-239 > prazosin suggest that [3H]rilmenidine binds to the .alpha.2A sub-type of adrenoceptor. Computer-resolved Ki values for drugs at the larger no. of lower affinity binding sites were very similar to Ki values detd. in the presence of 10 .mu.M adrenaline (used to block .alpha.2-adrenoceptor binding). The catecholamine-insensitive binding site did not share the pharmacol. characteristics of previously described, high affinity imidazoline-guanidinium receptive sites or high affinity imidazole sites, but more closely resembles the so-called "idazoxan receptor".

L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT **67339-62-2**, ARC-239
RL: PRP (Properties)
(affinity of, for rilmenidine binding sites in cerebral cortex)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:524363 CAPLUS
DOCUMENT NUMBER: 117:124363
TITLE: Discriminative stimulus effects of 8-OH-DPAT in pigeons: antagonism studies with the putative 5-HT1A receptor antagonists BMY 7378 and NAN-190
AUTHOR(S): Barrett, James E.; Gleeson, Suzanne
CORPORATE SOURCE: Med. Res. Div., American Cyanamid Co., Pearl River, NY, 10965, USA
SOURCE: Eur. J. Pharmacol. (1992), 217(2-3), 163-71
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pigeons were trained to discriminate 0.3 mg/kg of the 5-HT1A receptor agonist 8-hydroxy-2-(di-N-propylamino)tetralin (8-OH-DPAT) from saline. RU 24969 (5-methoxy-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indole), at doses of 5.6-10 mg/kg, and eltoprazine (5.6 mg/kg), both mixed 5-HT1A/B agonists, substituted completely for 8-OH-DPAT, whereas 3.0-10 mg/kg of the 5-HT 1B/C agonist TFMPP (1-(m-trifluoromethylphenyl)piperazine) and 0.1-3.0 of the 5-HT3 antagonist MDL 72222 (3-tropanyl-3,5-dichlorobenzoate) yielded only saline-appropriate responses. Substitution for 8-OH-DPAT by eltoprazine and RU 24969, which does not occur in rats, provides in vivo support for the suggestion that the absence of a 5-HT1B receptor in the pigeon allows more complete expression of 5-HT1A-mediated effects. BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]8-azaspiro1-[4.5]-decane-7,9-dione) attenuated the 8-OH-DPAT stimulus at doses from 1.0 to 10 mg/kg but, when administered alone, also resulted in approx. 40% 8-OH-DPAT-appropriate responding at the highest dose. NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalamido)butyl)-piperazine (0.3-3.0 mg/kg) produced a dose-dependent and complete antagonism of the 8-OH-DPAT-discriminative stimulus; administered alone NAN-190 resulted only in saline-key responding. NAN-190 also reversed the rate-decreasing effects of higher doses of 8-OH-DPAT. The .beta.-adrenoceptor antagonist (.+-.)-pindolol (5.6-17 mg/kg) antagonized the discriminative stimulus effects of lower 8-OH-DPAT doses but was unable to block the effects of higher doses of 8-OH-DPAT. Prazosin (1.0-10 mg/kg), which like NAN-190, is an .alpha.1-antagonist, neither substituted for nor blocked the discriminative stimulus effects of 8-OH-DPAT. These results suggest that NAN-190 is an effective 5-HT1A receptor antagonist in this procedure with

L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
pigeons with no indication of agonist actions, whereas BMY 7378 and pindolol are best characterized as partial 5-HT1A receptor agonists.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotoninergic S1A partial agonism by, in pigeons)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

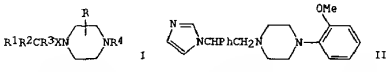


●2 HCl

L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:490321 CAPLUS
DOCUMENT NUMBER: 117:90321
TITLE: Piperazine derivatives
INVENTOR(S): Ward, Terence James; Warrellow, Graham John
PATENT ASSIGNEE(S): John Wyeth and Brother Ltd., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

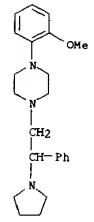
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 479546	A2	19920408	EP 1991-308969	19911001
EP 479546	A3	19920603		
EP 479546	B1	19961030		
R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
AU 9184883	A1	19920409	AU 1991-84883	19910930
AU 642532	B2	19931021		
US 5177078	A	19930105	US 1991-768147	19910930
GB 2248616	A1	19920415	GB 1991-20856	19911001
GB 2248616	B2	19940615		
JP 04257570	A2	19920911	JP 1991-253585	19911001
AT 144772	E	19961115	AT 1991-308969	19911001
ES 2094204	T3	19970116	ES 1991-308969	19911001
CA 2052619	AA	19920404	CA 1991-2052619	19911002
HU 59394	A2	19920528	HU 1991-3160	19911003
HU 217813	B	20000428		
IL 101166	A1	20000813	IL 1992-101166	19920306

PRIORITY APPLN. INFO.: GB 1990-21453 A 19901003
OTHER SOURCE(S): MARPAT 117:90321
GI

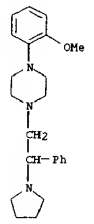


AB Piperazines I (X = alkylene; R = H, alkyl; R1, R4 = aryl, heteroaryl; R2 = mono- or bicyclic heterocyclic; R3 = H, OH, alkyl) were prepd. Thus, 1-(2-methoxyphenyl)piperazine was treated with styrene oxide followed by imidazole to give the piperazine II. II had 5-hydroxytryptamine type 1A receptor antagonist activity in rats at a min. ED of 1 mg/kg s.c. and 10 mg/kg orally.
IT **141733-67-7P 142234-29-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 141733-67-7 CAPLUS
CN Piperazine, 1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]- (9CI) (CA INDEX NAME)



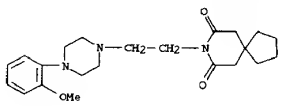
RN 142234-29-5 CAPLUS
CN Piperazine, 1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:483356 CAPLUS
DOCUMENT NUMBER: 117:83356
TITLE: Evidence for postsynaptic mediation of the hypothermic effect of 5-HT1A receptor activation
AUTHOR(S): O'Connell, M. T.; Sarna, G. S.; Curzon, G.
CORPORATE SOURCE: Dep. Neurochem., Inst. Neurol., London, WC1N 3BG, UK
SOURCE: Br. J. Pharmacol. (1992), 106(3), 603-9
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-HT1A ligand BMY 7378 (8-[2[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]8-azaspiro [4,5]-decane-7,9-dione dihydrochloride, 0.032-2 mg kg-1, s.c.) caused hyperphagia, a response to the activation of presynaptic 5-HT1A receptors. BMY 7378 (8 mg kg-1, s.c.) and the 5-HT1A agonist (8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), 0.10 and 0.25 mg kg-1 s.c.) also caused hypothermia. This was inhibited by (-)-pindolol (1 mg kg-1, i.p.) and not prevented by pretreatments with p-chlorophenylalanine which grossly depleted 5-hydroxytryptamine (5-HT) from terminal regions. The hypothermic effects are explicable by activation of postsynaptic 5-HT1A receptors. Infusion of BMY 7378 (8-64 .mu.g) into the dorsal raphe was without convincing hypothermic effect. BMY 7378 (8 mg kg-1), s.c.) inhibited another effect of activation of postsynaptic 5-HT1A receptors, i.e., the induction of components of the 5-HT syndrome by 8-OH-DPAT (0.5, 1.0 mg kg-1, s.c.) which suggests that BMY 7378 has antagonistic as well as agonistic effects at there sites. Partial agonist properties of BMY 7378 at postsynaptic sites were also indicated by doses for hypothermia being much greater than those for hyperphagia i.e., ED50 (hypothermia)>2 mg kg-1, ED50 (hyperphagia) = 0.010 mg kg-1. This contrasts with the similar ED50 values for both the hypothermic (ED50 = 0.08-0.10 mg kg-1) and hyperphagic (ED50 = 0.06-0.10 mg kg-1) effects of 8-OH-DPAT. The evidence obtained for mediation of the hypothermic response to 5-HT1A agonists by postsynaptic sites is relevant to the interpretation of the effect on it of antidepressant treatments and depressive illness.
IT **21102-95-4**, BMY 7378
RL: FRP (Properties)
(hypothermic and hyperphagic and behavioral effects of, serotonergic S1A receptors in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

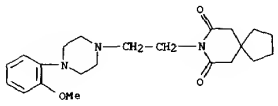
L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 169 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:420443 CAPLUS
DOCUMENT NUMBER: 117:20443
TITLE: The putative 5-HT1A antagonist BMY 7378 blocks 8-OH-DPAT-induced changes in local cerebral glucose utilization in the conscious rat
AUTHOR(S): Grasby, P. M.; Sharp, T.; Allen, T.; Grahame-Smith, D. G.
CORPORATE SOURCE: Univ. Dep. Clin. Pharmacol., Radcliffe Infirm., Oxford, OX2 6HE, UK
SOURCE: Neuropharmacology (1992), 31(6), 547-51
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has previously been shown that the 5-HT1A agonist, 8-OH-DPAT, caused discrete changes in cerebral glucose utilization in the rat, as assessed by quant. 2-deoxyglucose autoradiog. Here, the effect of the putative 5-HT1A antagonist, BMY 7378, on regional cerebral glucose utilization was examd., when injected alone and in rats treated with 8-OH-DPAT. In control rats, BMY 7378 (5 mg/kg, s.c.) markedly increased glucose utilization in the lateral habenular nucleus and moderately reduced glucose utilization in the hippocampal formation. Pretreatment with BMY 7378 (5 mg/kg) significantly attenuated the redns. in glucose utilization in the hippocampus, entorhinal, piriform and cingulate cortex, induced by 8-OH-DPAT (0.25 mg/kg). The 8-OH-DPAT-induced increase in glucose utilization in the copula pyramis, that is putatively assocd. with the appearance of the 5-HT behavioral syndrome, was also blocked by BMY 7378, as was the behavioral syndrome. In summary, BMY 7378 produced few of the discrete changes in cerebral glucose utilization that are seen with 8-OH-DPAT. However, many of the changes induced by 8-OH-DPAT were reversed by BMY 7378. These data are consistent with the hypothesis that the effects of 8-OH-DPAT on regional cerebral glucose utilization are mediated by 5-HT1A receptors.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(8-OH-DPAT-induced brain regional glucose utilization blockade by, serotonin S1A receptors in)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 169 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



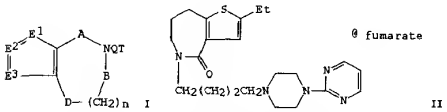
●2 HCl

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:194290 CAPLUS
DOCUMENT NUMBER: 116:194290
TITLE: Preparation of thienoazepinone compounds and their use as drugs
INVENTOR(S): Nakao, Tohru; Tanaka, Hiroshi; Yamato, Hirotake; Akagi, Takeshi; Takehara, Shuzo
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 74 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 465254	A1	19920108	EP 1991-306095	19910704
EP 465254	B1	19961113		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 05043582	A2	19930223	JP 1991-191087	19910704
AT 145208	E	19961115	AT 1991-306095	19910704
CA 2046368	AA	19920107	CA 1991-2046368	19910705
US 5141930	A	19920825	US 1991-726683	19910708

PRIORITY APPLN. INFO.: JP 1990-179953 19900706
JP 1990-232244 19900831
JP 1990-326644 19901127
JP 1991-13684 19910111
JP 1991-75657 19910314
OTHER SOURCE(S): MARPAT 116:194290
GI



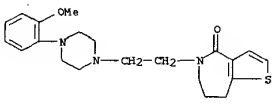
AB Title compds. I [one of E1, E2, E3 is S and the other 2 are R1C, R2C wherein R1, R2 = H, halo, O2N, H2N, cyano, HO, CHO, alkyl, alkoxy, haloalkyl, (substituted) H2NSO2, alkylthio, HO2C, etc.; D = CH2, S(O)m wherein m = 0-2; Q = alkylene: T = amino, heterocyclyl; A = CO, CS, CH2; B = CO, CS] or a salt thereof, useful as antianxietics, antipsychotics and for treatment of circulatory disorders, are prepd. 2-Acetyl-5-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl-5,6,7,8-tetrahydro-4H-thieno[3,2-c]azepin-4-one (prepn. given) in F3CCO2H was added Et3SiH, the mixt. stirred for 20

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

h at room temp to give after work-up and addn. of fumaric acid the thienoazepinone II. In the receptor binding test, the Ki (nM) of II for 5-HT1A, 5-HT2, and D2 was 1.3, 990.0 and 78.0, resp., and the anxiolytic effect was (min. ED) .ltoreq.1.0 mg/kg, p.o. Addn. I were prepd. and tested. A tablet formulation comprising I is given.

IT **140217-04-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

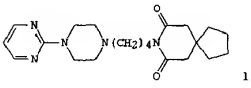
RN 140217-04-5 CAPLUS
CN 4H-Thieno[3,2-c]azepin-4-one, 5,6,7,8-tetrahydro-5-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L14 ANSWER 171 OF 263 CAPLUS COPYRIGHT 2002 ACS

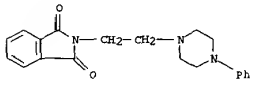
ACCESSION NUMBER: 1992:193385 CAPLUS
DOCUMENT NUMBER: 116:193385
TITLE: Unexpected configuration of molecules of buspirone and its analogs in solution
AUTHOR(S): Bondarev, M. L.; Kalyuskii, A. R.; Shapiro, Yu. E.; Andronati, S. A.
CORPORATE SOURCE: Fiz.-Khim. Inst., Odessa, USSR
SOURCE: Ukr. Khim. Zh. (Russ. Ed.) (1991), 57(9), 986-91
CODEN: UKZHAU; ISSN: 0041-6045
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI



AB NMR results for buspirone (I) and several analogs in CD2Cl2, including spin-lattice relaxation times and Overhauser effects, indicated that a nearly chelate structure was preferred, possibly because of dipole-dipole interaction.

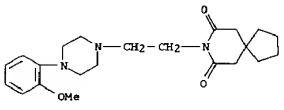
IT **75000-24-7**
RL: PRP (Properties)
(conformation of, NMR in relation to)

RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:143745 CAPLUS
DOCUMENT NUMBER: 116:143745
TITLE: Antagonism studies with BMY-7378 and NAN-190: effects
on 8-hydroxy-2-(di-n-propylamino)tetralin-induced increases in punished responding of pigeons
AUTHOR(S): Ahlers, Stephen T.; Weissman, Ben Avi; Barrett, James E.
CORPORATE SOURCE: Neurochem. Div., Nav. Med. Res. Inst., Bethesda, MD, USA
SOURCE: J. Pharmacol. Exp. Ther. (1992), 260(2), 474-81
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purported serotonin (5-HT)1A antagonists BMY-7378 and NAN-190 were examd. in pigeons for their potential to block the effects of the prototypical 5-HT1A agonist 8-OH-DPAT on punished ("conflict") and unpunished behavior and for their binding affinity at the 5-HT1A receptor site labeled by [3H]-8-OH-DPAT. Although BMY-7378 and NAN-190 both displayed high affinity for the 5-HT1A receptor (IC50 values of 0.8 and 7.5 nM, resp.), their effects, when administered alone, as well as in combination with 8-OH-DPAT, were distinct. 8-OH-DPAT (0.3-3.0 mg/kg) produced large increases in punished responding at doses that did not affect or that decreased unpunished responding. Administration of NAN-190 (1.0-3.0 mg/kg) did not increase punished responding, whereas BMY-7378 (1.0-5.6 mg/kg) slightly increased behavior suppressed by punishment. Pretreatment with BMY-7378 attenuated the rate-increasing effects of 8-OH-DPAT on punished responding; however, these effects were accompanied by dose-dependent enhancement of the rate-decreasing effects of 8-OH-DPAT on unpunished responding. In contrast, NAN-190 blocked the rate-increasing effects of 8-OH-DPAT on punished responding and also reversed the rate-decreasing effects of 8-OH-DPAT on responding that was not punished. Pretreatment with NAN-190 failed to block increases in punished responding produced by 0.1 to 1.9 mg/kg of the benzodiazepine midazolam. These data suggest that NAN-190 may be characterized as an antagonist and BMY-7378 a partial agonist with respect to 5-HT1A-induced behavioral changes obsd. in the conflict procedure with pigeons.
IT **21102-95-4**, BMY-7378
RL: B10L (Biological study)
(serotoninergic S1A receptor binding by, as partial agonist, in brain cerebrum, conflict behavior response to)
RN 21102-95-4 CAPLUS

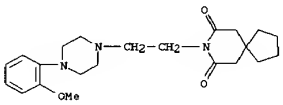
L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:143743 CAPLUS
DOCUMENT NUMBER: 116:143743
TITLE: The putative 5-HT1A receptor antagonists NAN-190 and BMY 7378 are partial agonists in the rat dorsal raphe nucleus in vitro
AUTHOR(S): Greuel, Joachim M.; Glaser, Thomas
CORPORATE SOURCE: Inst. Neurobiol., Troponwerke G.m.b.H. und Co. K.-G., Cologne, D-5000/80, Germany
SOURCE: Eur. J. Pharmacol. (1992), 211(2), 211-19
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present electrophysiol. study examd. the actions of the putative 5-HT1A receptor antagonists, NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine-HBr) and BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro(4,5]dione-7,9-dione-2HCl) in the rat dorsal raphe nucleus in vitro. There was no major difference between the effects of the two drugs on any measure investigated. Both compds. reduced neuronal activity in a concn.-dependent manner, with BMY 7378 being slightly more potent than NAN-190. The threshold concns. eliciting inhibitory effects were 1 nM for BMY 7378 and 3 nM for NAN-190. Complete inhibition occurred at concns. close to 30 nM. The effects of the 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-2-(dipropylamino)tetralin) could be antagonized when concns. of NAN-190 or BMY 7378 were used that were too low to produce a marked inhibition. At concn. close to threshold both compds. potentiated the inhibitory effects of 3 nM 8-OH-DPAT. The suppression of neuronal firing induced by NAN-190 and BMY 7378 could be completely antagonized with propranolol, indicating that the inhibitory actions of both drugs were not primarily due to .alpha.1-adrenoceptor antagonism. By applying theorems of receptor theory, the intrinsic activities for both NAN-190 and BMY 7378 were calcd. to be in the range of 0.1-0.3. Thus, NAN-190 and BMY 7878 are partial agonists in the rate dorsal raphe nucleus. The results can be best explained by assuming that a crit. threshold of receptor occupancy has to be reached in order to elicit a biol. response and by assuming a receptor reserve that may account for the apparent full agonism of NAN-190 and BMY 7378.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotoninergic S1A antagonistic and partial agonistic activity of, in brain dorsal raphe nucleus)

L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

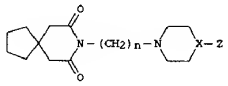


●2 HCl

L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:41481 CAPLUS
DOCUMENT NUMBER: 116:41481
TITLE: Preparation of new piperazine- and piperidine-containing azaspiro[4.5]decane-7,9-dione derivatives with serotoninergic activity
INVENTOR(S): Orjales Venero, Aurelio; Rodes Solanes, Rosa
PATENT ASSIGNEE(S): Fabrica Espanola de Productos Quimicos y Farmaceuticos S. A. (FAES), Spain
SOURCE: Span., 8 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2019228	A6	19910601	ES 1990-421	19900213
FI 9100652	A	19910814	FI 1991-652	19910211
EP 447345	A2	19910918	EP 1991-500014	19910211
EP 447345	A3	19920415		
R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE				
NO 9100564	A	19910814	NO 1991-564	19910212
AU 9170983	A1	19910815	AU 1991-70983	19910212
CA 2036269	AA	19910814	CA 1991-2036269	19910213
JP 08092221	A2	19960409	JP 1991-41144	19910213

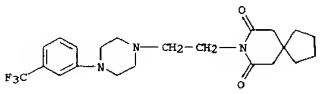
PRIORITY APPLN. INFO.: ES 1990-421 19900213
OTHER SOURCE(S): MARPAT 116:41481
GI



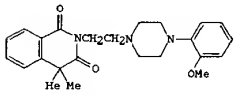
I

AB Title compds. I [X = N, CH; n = 2 or 4; Z = pyrimidin-2-ylamino, 3-F3CC6H4, or benzimidazol-2-yl substituted in 1-position by lower alkyl or 4-FC6H4CH2] are prepd. by cyclocondensation of 3,3-tetramethyleneglutaric anhydride (II) with corresponding amines in, e.g., pyridine, PhMe, or BuOH, at 80-140.degree., preferably at reflux temp. Thus, reaction of II with 1-(4-aminobutyl)-4-[3-(trifluoromethyl)phenyl]piperazine in refluxing pyridine over 20 h gave 66% I (X = N, n = 4, Z = 3-F3CC6H4). I showed 5-HT1A receptor activity (displacement of [3H]-8-OH-DPAT from rat frontal cortex tissue) similar to

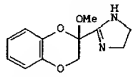
L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
buspirone (Ki = 1.99 .times. 10-8).
IT **138307-27-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as nervous system agent)
RN 138307-27-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:671300 CAPLUS
DOCUMENT NUMBER: 115:271300
TITLE: Delineation of three pharmacological subtypes of .alpha.2-adrenoceptor in the rat kidney
AUTHOR(S): Uhlen, Staffan; Wikberg, Jarl E. S.
CORPORATE SOURCE: Dep. Pharmacol., Umea Univ., Umea, S-901 87, Swed.
SOURCE: Br. J. Pharmacol. (1991), 104(3), 657-64
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



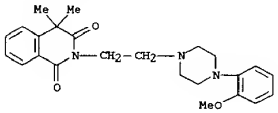
I



II

AB Simultaneous computer modeling of plain and ARC 239 (I)- and guanoxabenz-masked [3H]-RX 821002 (II) satn. curves, plain I and guanoxabenz competition curves as well as I-masked guanoxabenz competition curves revealed that the drugs bound to three .alpha.2-adrenoceptor subtypes in the rat kidney with grossly differing selectivities. These .alpha.2-adrenoceptor subtypes were termed .alpha.2A, .alpha.2B1, and .alpha.2B2. The order of affinities for [3H]II for the adrenoceptor sites was .alpha.2A > .alpha.2B1 > .alpha.2B2, the Kds being 0.62, 2.25, and 6.74 nM, resp. The order of affinities for I was .alpha.2B1 > .alpha.2B2 .mchgt. .alpha.2A with Kds 4.78, 28.8, and 1460 nM, resp. For guanoxabenz the order of affinities was .alpha.2A > .alpha.2B1 .mchgt. .alpha.2B2 with Kds 99.7, 508, and 25,400 nM, resp. The affinities of guanoxabenz for .alpha.2B1- and .alpha.2B2-adrenoceptors differed 72-fold and for .alpha.2A- and .alpha.2B2-adrenoceptors 380-fold. The selectivities of a no. of other drugs were less marked but their Kds were consistent with all 3 sites being .alpha.2-adrenoceptors. (-)-Adrenaline and (-)-noradrenaline showed dissimilar order of affinities for the three .alpha.2-adrenoceptors. For (-)-adrenaline the order of affinities was .alpha.2B1 .gtoreq. .alpha.2A > .alpha.2B2 and for (-)-noradrenaline

L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
.alpha.2B2 .gtoreq. .alpha.2B1 > .alpha.2A. All three .alpha.2-adrenoceptors showed the expected stereoselective binding for adrenaline enantiomers, the (+)-form being 7-10-fold less potent than the (-)-form. [3H]yohimbine was also used as radioligand. The data with this ligand were fully compatible with the [3H]II data. However, [3H]yohimbine appeared to label only .alpha.2B1- and .alpha.2B2-adrenoceptors presumably because it had too low an affinity for .alpha.2A-adrenoceptors. Apparently, 3 pharmacol. subtypes of .alpha.2-adrenoceptors are labeled by [3H]II in the rat kidney. Guanoxabenz and ARC 239 may be used in competition studies to delineate between these three .alpha.2-adrenoceptor subtypes.
IT **67339-62-2**, ARC-239
RL: BIOL (Biological study)
(.alpha.2-adrenergic receptor classification with, in kidney)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS

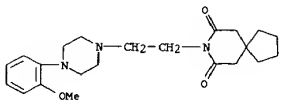
ACCESSION NUMBER: 1991:598360 CAPLUS
DOCUMENT NUMBER: 115:198360
TITLE: Effects of serotonergic agents on isolation-induced aggression
AUTHOR(S): White, Sheryl M.; Kucharik, Robert F.; Moyer, John A.
CORPORATE SOURCE: CNS Div., Wyeth-Ayerst Res., Princeton, NJ, 08543-8000, USA
SOURCE: Pharmacol., Biochem. Behav. (1991), 39(3), 729-36
CODEN: PBBHAU; ISSN: 0091-3057
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of serotonergic agents were assessed for their ability to antagonize isolation-induced aggression and disrupt performance in the rotorod motor coordination test. All compds. with 5-HT1A activity [buspirone, gepirone, ipsapirone, tandospirone (SM-3997), 8-OH-DPAT, Wy48,723, BMY7378, Wy47,846] reduced aggression at doses below those which produced debilitation in the rotorod motor coordination test. In addn., the 5-HT3 antagonist zacopride failed to attenuate aggression or produce debilitation at any of the doses tested; however, the 5-HT2 antagonist ritanserin inhibited aggressive behavior at a high dose which was not debilitating. Benzodiazepines (chlordiazepoxide, diazepam and lorazepam), and an antidepressant (desipramine) and an antipsychotic (haloperidol) reduced aggressive behavior only at debilitating doses. Activity at the 5-HT1A receptor, and possibly nonsedative anxiolytic activity, appears to be related to antagonism of isolation-induced aggression.

IT **21102-95-4**, BMY-7378
RL: BIOL (Biological study)
(isolation-induced aggression response to, serotoninergic mechanisms in)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



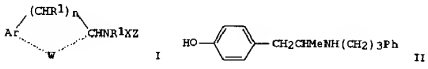
●2 HCl

L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:582801 CAPLUS
DOCUMENT NUMBER: 115:182801
TITLE: Preparation of substituted phenylisopropylamines and analogs as sigma receptor ligands for treatment of schizophrenia and psychoses
INVENTOR(S): Glennon, Richard A.
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9109594	A1	19910711	WO 1990-US7653	19901228
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CH, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2071897	AA	19910629	CA 1990-2071897	19901228
AU 9171684	A1	19910724	AU 1991-71684	19901228
AU 658134	B2	19950406		
EP 507863	A1	19921014	EP 1991-902640	19901228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503517	T2	19930610	JP 1991-502935	19901228
PRIORITY APPLN. INFO.:			US 1989-459061	19891228
			WO 1990-US7653	19901228

OTHER SOURCE(S): MARPAT 115:182801
GI



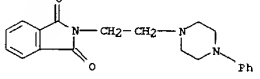
AB Title compds. I [Ar = (substituted) aryl or heteroaryl; R = H, C1-6 alkyl; R1 = H, C1-6 alkyl, C1-6 alkoxy, Br, Cl, F, O; or RR1 = morpholine, piperazinyl, piperidinyl; n = 0-5; W = (CH2)p, 2H; p = 1-3; X = (CH2)q; q = 1-6, (CH2)rC.tplbond.C(CH2)r, (CH2)rCH:CH(CH2)r, (CH2)rCO(CH2)r, (CH2)rY(CH2)r; r = 0-3; Y = O, S, C1-6 alkyl; Z = H, (substituted) aryl or heteroaryl], are prepd. PhCH2CH2CHO and (R)-(-)-PhCH2CH(NH2)Me in MeOH were hydrogenated over Pt/C at room temp. to give (R)-N-(3-phenylpropyl)-1-

L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

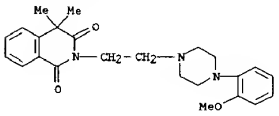
phenyl-2-aminopropane. Also prepd. was the (.+-.)-amine II.HBr (III). In sigma receptor binding assays the IC50 of III was 1.03 .times. 10-8 M. I were subjected to sigma, PCP and dopamine receptor binding assays and the results showed very high binding to sigma receptor and very low binding to PCP and DA receptors, and thus I are useful for treatment of mental illness (no data) without the extrapiramidal side effects of traditional neuroleptic agents caused by binding to DA receptor.

IT **75000-24-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as sigma receptor ligand)

RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

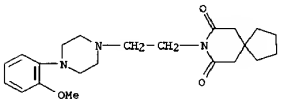


L14 ANSWER 178 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:551496 CAPLUS
DOCUMENT NUMBER: 115:151496
TITLE: Identification and characterization of .alpha.2D-adrenergic receptors in bovine pineal gland
AUTHOR(S): Simonneaux, V.; Ebadi, M.; Bylund, D. B.
CORPORATE SOURCE: Med. Cent., Univ. Nebraska, Omaha, NE, 68198-6260, USA
SOURCE: Mol. Pharmacol. (1991), 40(2), 235-41
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using [3H]rauwolscine, a selective .alpha.2-adrenergic receptor antagonist, .alpha.2-adrenergic receptor sites were identified in a mammalian pineal gland. [3H]Rauwolscine bound in a saturable manner to a single class of receptors, with an equil. dissocn. const. of 1.4 nM and a d. of 71 fmol/mg of protein, in crude synaptic membrane prepns. from bovine pineal gland. Competition studies carried out with various adrenergic antagonists supported the conclusion that [3H]rauwolscine-binding sites were .alpha.2-adrenergic receptors. The bovine pineal .alpha.2-adrenergic receptor appears to represent a pharmacol. subtype distinct from the 3 currently proposed subtypes, i.e., .alpha.2 found in a human colonic adenocarcinoma cell line (HT29 cell) .alpha.2B found in rat lung, and .alpha.2C found in an opossum kidney cell line. However, the pharmacol. profile of the pineal .alpha.2 receptor resembles that found in the rat submaxillary gland. The bovine pineal receptor may represent a 4th pharmacol. subtype, which would be designated as .alpha.2D.
IT **67339-62-2**, ARC-239
RL: BIOL (Biological study)
(.alpha.2D-adrenergic receptor binding by, in pineal gland)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:528127 CAPLUS
DOCUMENT NUMBER: 115:128127
TITLE: Single-dose 8-OH-DPAT pretreatment does not induce tachyphylaxis to the 5-HT release-reducing effect of 5-HT1A autoreceptor agonists
AUTHOR(S): Hjorth, Stephan
CORPORATE SOURCE: Dep. Pharmacol., Univ. Goteborg, Goteborg, S-400 33, Swed.
SOURCE: Eur. J. Pharmacol. (1991), 199(2), 237-42
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has recently been suggested that central 5-HT1A autoreceptors are already desensitized after single-does 5-HT1A agonist treatment. In turn, this would lead to an attenuated feedback suppression of transmitter release from 5-HT neurons, and thus to enhanced 5-HT synaptic transmission. In vivo brain microdialysis techniques were used in an attempt to test this hypothesis. Single-dose pretreatment with the ref. 5-HT1A receptor agonist 8-hypoxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT, did not alter the baseline output of 5-HT in the rat ventral hippocampus 24 h later, and did not alter the release-reducing response to 5-HT1A agonist (8-OH-DPAT, ipsapirone or BMY 7378) challenge under the same conditions. Thus, the functional responsiveness of the 5-HT release-controlling 5-HT1A autoreceptors is maintained after bolus 8-OH-DPAT pretreatment. When related to the acute 8-OH-DPAT-induced redn. in raphe 5-HT1A radioligand binding d. recently reported by others, the present results are consistent with a large functional overcapacity of this 5-HT1A receptor population. The mechanism by which 5-HT1A receptor-mediated hypothermia and hyperphagia are rapidly attenuated by a previous large single dose of a 5-HT1A receptor agonist remains to be explained.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotonin release by hippocampus response to, receptor desensitization in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

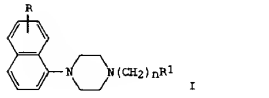


●2 HCl

L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:514553 CAPLUS
DOCUMENT NUMBER: 115:114553
TITLE: 1-naphthylpiperazine derivatives, process for their preparation and pharmaceutical compositions containing them
INVENTOR(S): Lavielle, Gilbert; Laubie, Michel; Colpaert, Francis
PATENT ASSIGNEE(S): ADIR et Cie., Fr.
SOURCE: Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

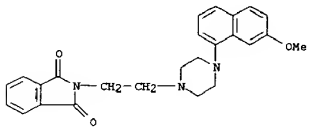
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 434561	A2	19910626	EP 1990-403688	19901220
EP 434561	A3	19910918		
EP 434561	B1	19951018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2655988	A1	19910621	FR 1989-16882	19891220
FR 2655988	B1	19940520		
ZA 9009767	A	19911127	ZA 1990-9767	19901205
CA 2032713	AA	19910621	CA 1990-2032713	19901219
AU 9068235	A1	19910627	AU 1990-68235	19901219
AU 635369	B2	19930318		
JP 03291275	A2	19911220	JP 1990-403922	19901219
JP 06076395	B4	19940928		
US 5143916	A	19920901	US 1990-629824	19901219
AT 129241	E	19951115	AT 1990-403688	19901220
ES 2080815	T3	19960216	ES 1990-403688	19901220
US 5166157	A	19921124	US 1991-750821	19910827
US 5162324	A	19921110	US 1991-752060	19910829
US 5162321	A	19921110	US 1991-752063	19910829
US 5166156	A	19921124	US 1991-752065	19910829

PRIORITY APPLN. INFO.: FR 1989-16882 19891220
US 1990-629824 19901219
OTHER SOURCE(S): MARPAT 115:114553
GI



I

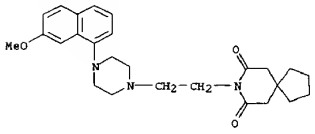
L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
AB Naphthylpiperazines I [n = 1-4; R = H, halogen, OH, alkyl, alkoxy; R1 =
NHCOR2, NHSO2R3, NHCONHR4, (un)substituted phthalimido, benzisothiazole
dioxide, NBz2, imidazopyrimidinyl, azaspirodecyl; R2 = alkyl, cycloalkyl,
Ph, substituted Ph, heteroaryl; R3 = alkyl, cycloalkyl, Ph, substituted
Ph; R4 = alkyl, Ph, substituted Ph] were prepd. by various methods. Thus
7-methoxy-1-naphthylpiperazine was treated with BrCH2CN, followed by redn.
to the 2-aminoethyl deriv. and acylation to give I (n = 2, R = 7-OMe, R1 =
4-FC6H4CONH) which had better antihypertensive and neg. chronotropic
activity than flesinoxan.
IT **135722-16-6P 135722-24-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 135722-16-6 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(7-methoxy-1-naphthalenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 135722-24-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(7-methoxy-1-naphthalenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



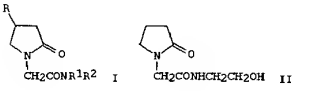
●x HCl

L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:492061 CAPLUS
DOCUMENT NUMBER: 115:92061
TITLE: Preparation of 2-pyrrolidone derivatives as enhancers
for learning and memory
INVENTOR(S): Giannessi, Fabio; Ghirardi, Orlando; Misiti, Domenico;
Tinti, Maria Ornella; Scolastico, Carlo
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 408524	A1	19910116	EP 1990-830317	19900710
EP 408524	B1	19951108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, LI, LU, NL, SE				
AT 129996	E	19951115	AT 1990-830317	19900710
ES 2079469	T3	19960116	ES 1990-830317	19900710
JP 03048657	A2	19910301	JP 1990-185173	19900711
US 5061725	A	19911029	US 1990-551951	19900712

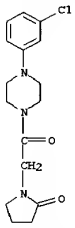
PRIORITY APPLN. INFO.: IT 1989-48180 19890712
OTHER SOURCE(S): MARPAT 115:92061
GI



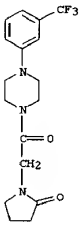
I II

AB The title compds. I [R = H, OH; R1 = H; R2 = 2-aminoethyl, 2-(diisopropylamino)ethyl, 2-hydroxyethyl, etc.] were prepd. A mixt. of
Me (2-oxopyrrolidin-1-yl)acetate and ethanolamine was stirred at room temp. for 20 h to give pyrrolidone deriv. II. I (R = R1 = H; R2 = CH2CH2NH2) had memory-enhancing activity equal to that of piracetam.
IT **131028-02-9P 135459-98-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as memory enhancer)
RN 131028-02-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-(9CI)
(CA INDEX NAME)

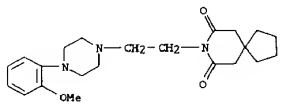
L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 135459-98-2 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[3-(trifluoromethyl)phenyl]-(9CI) (CA INDEX NAME)



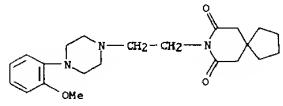
L14 ANSWER 182 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:485329 CAPLUS
DOCUMENT NUMBER: 115:85329
TITLE: BMY 7378 is an agonist at 5-HT1A receptors mediating hypotension and renal sympatho-inhibition in anesthetized cats
AUTHOR(S): Stubbs, Carole M.; Connor, Helen E.; Feniuk, Wasyl
CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Hertfordshire, SG12 ODJ, UK
SOURCE: Eur. J. Pharmacol. (1991), 197(1), 113-16
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The putative 5-HT1A receptor antagonist BMY 7378 (3-100 .mu.g.cntdot.kg-1 i.v.) caused redns. in blood pressure, heart rate and efferent renal nerve activity in anesthetized cats. Similar effects were produced by the selective 5-HT1A receptor agonist, 8-hydroxy-2(di-n-propylamino)tetralin (8-OH-DPAT 1-10 .mu.g.cntdot.kg-1 i.v.). The sympatho-inhibitory effects of BMY 7378 and 8-OH-DPAT, but not those of clonidine were reversed by the non-selective 5-HT1A receptor antagonist, spiperone (1 mg.cntdot.kg-1 i.v.). It is concluded that BMY 7378 is an agonist at 5-HT1A receptors mediating hypotension and renal sympatho-inhibition in anesthetized cats.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(as serotoninergic S1A receptor agonist, cardiovascular and renal sympathetic nerve response to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:221898 CAPLUS
DOCUMENT NUMBER: 114:221898
TITLE: 5-Hydroxytryptamine (5-HT)1A receptors and the tail-flick response. I. 8-Hydroxy-2-(di-n-propylamino)tetralin hydrobromide-induced spontaneous tail-flicks in the rat as an in vivo model of 5-HT1A receptor-mediated activity
AUTHOR(S): Millan, Mark J.; Bervoets, Karin; Colpaert, Francis C.
CORPORATE SOURCE: Neurobiol. Div., Fondaw, Puteaux, 92800, Fr.
SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 973-82
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study characterizes a novel behavioral response as a potential in vivo model of 5-HT1A receptor-mediated activity. In rats restrained in horizontal cylinders, the selective 5-HT1A agonist 8-hydroxy-2-(dipropylamino)tetralin-HBr (8-OH-DPAT) dose-dependently (0.04-10.0 mg/kg, s. c.) elicited spontaneous tail-flicks (STFs). This action was mimicked by other ligands possessing high affinity and high efficacy at 5-HT1A sites: RU 24969, lisuride, (+)-LSD, and 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate. The response could not be elicited by CGS 12066B, mCPP [1-(3-chlorophenyl)-piperazine-2-HCl], TFMPP, MK 212, quipazine, and (.+-.)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl, which act in vivo as agonists at 5-HT1B, 5-HT1C and(or) 5-HT2 receptors, or by the 5-HT3 agonist, 2-methyl-5-HT. p-Chloroamphetamine, which releases endogenous 5-HT, also evoked STFs; in contrast, d-amphetamine, a preferential releaser of catechlroamines, was inactive as were agonists and antagonists at .alpha.1-, .alpha.2-, .beta.1-, .beta.2-, and dopamine D1 and D2 sites. 8-OH-DPAT-elicited STFs were blocked by the 5-HT1/2 antagonist, methiothepin, but not by the 5-HT1C/5-HT2 antagonists, mianserin, ritanserin, and ICI 169,369 nor by the 5-HT3 antagonists, GR 38032F, ICS 205,930, and MDL 72222. .beta.-Blockers with high 5-HT1A affinity i.e., (-)alprenolol, (.+-.)-isamoltane and, stereoselectively, (-)- but not (+)-pindolol, blocked the action of 8-OH-DPAT. Spiperone and spiroxatrine, D2 antagonists with high 5-HT1A affinity, also inhibited 8-OH-DPAT-induced STFs. Selective .beta.-blockers and D2 antagonists with low 5-HT1A affinity were inactive. 5-HT1A partial agonists, the pyrimidinylpiperazines buspirone, gepirone, and ipsapirone, the halogenated phenylpiperazine LY 165,163, and the benzodioxan MDL 72832 did not elicit STFs and antagonized the effect of 8-OH-DPAT. The

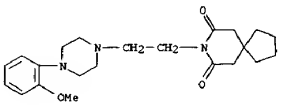
L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
heterobicyclic arylpiperazine selective 5-HT1A ligand, (.+-.)-flesinoxan, also failed to evoke STFs and attenuated the action of 8-OH-DPAT. The novel, putative 5-HT1A antagonists, BMY 7378 and NAN 190, abolished the action of 8-OH-DPAT and p-chloroamphetamine. Thus, a high efficacy agonist action at 5-HT1A receptors is sufficient for the induction of STFs in the rat. This response offers a novel, robust, and quant. test for the in vivo characterization of drugs acting at 5-HT1A receptors.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotoninergic S1A agonist-induced tail flick behavior antagonism by)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

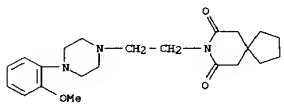
L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:178855 CAPLUS
DOCUMENT NUMBER: 114:178855
TITLE: 5-Hydroxytryptamine (HT)1A receptors and the tail-flick response. II. High efficacy 5-HT1A agonists attenuate morphine-induced antinociception in mice in a competitive-like manner
AUTHOR(S): Millan, M. J.; Colpaert, F. C.
CORPORATE SOURCE: Neurobiol. Div., Fondax, Puteaux, 92800, Fr.
SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 983-92
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. the influence of s.c. administration of HT1A agonists upon the antinociceptive action of s.c injected morphine in tail-flick tests to noxious heat and pressure. The selective 5-HT1A agonist, (.+-.)-8-hydroxy-dipropylaminotetralin-Br (8-OH-DPAT), dose-dependently antagonized morphine-induced antinociception (MIA) without affecting the latency to respond when applied alone. In the presence of increasing doses of 8-OH-DPAT (0.16-0.63 mg/kg), the morphine dose-response curve was shifted progressively in parallel to the right and the maximal effect of morphine was not altered; Schild anal. yielded a slope of close to -1.0. 8-OH-DPAT both prevented and reversed the action of morphine. The action of 8-OH-DPAT was reversible (at 24 h). In contrast, 8-OH-DPAT neither blocked morphine-induced Straub tail nor pptd. withdrawal in morphine-dependent animals; thus, it lacked opioid-antagonist properties. The antagonism of MIA by 8-OH-DPAT was mimicked by addnl. drugs acting as high efficacy 5-HT1A agonists: lisuride, 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate, RU 24969 and d-LSD. In contrast, the 5-HT1B/1C agonist TFMPP and the 5-HT1C/2 agonist (.+-.)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl were ineffective. The putative selective 5-HT1A antagonists BMY 7378 and spiperone did not reduce MIA. Indeed, BMY 7378 blocked the ability of 8-OH-DPAT to antagonize MIA. Under the present conditions, agonists and antagonists at adrenergic and dopaminergic receptors did not attenuate MIA. These data show that, over a certain range of doses, the systemic administration of 8-OH-DPAT and other high efficacy 5-HT1A agonists functionally antagonizes the antinociceptive action of systemically applied morphine in a competitive-like manner. It is suggested that 5-HT1A receptors play an important role in the modulation of opioidergic antinociceptive mechanisms.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)

L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(serotoninergics S1A agonist antagonism of morphine analgesia blockade
by)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 185 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:178780 CAPLUS
DOCUMENT NUMBER: 114:178780
TITLE: Differential behavior activation following intra-raphe
infusion of 5-HT1A receptor agonists
AUTHOR(S): Higgins, Guy A.; Elliott, Peter J.
CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Herfordshire, SG12 0DP, UK
SOURCE: Eur. J. Pharmacol. (1991), 193(3), 351-6
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microinfusion of the selective 5-HT1A receptor agonist, 8-hydroxy-(di-N-propylamino)tetralin (8-OHDPAT), into the dorsal raphe nucleus (DRN) produced a marked behavioral hypoactivity and flat body posture. Injections of similar doses into the median raphe nucleus (MRN)
elicited hyperactivity but no postural change. RednS. in rearing and grooming were also obsd. after DRN and MRN infusions of 8-OHDPAT. The behavioral profiles of other 5-HT1A selective compds., gepirone and BMY7378 were found to be similar to 8-OHDPAT. The contrasting behavioral
profiles of the 5-HT1A agents obsd. after DRN or MRN microinfusion are probably related to the differential innervation of forebrain structures
by each raphe nucleus. Thus, the present data confirms and extends previous results illustrating the influence of 5-HT systems on motor behavior in the rat and identifies unique behavioral profiles following
activation of the DRN and MRN.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(behavior response to intra-raphe administration of, serotonergic mechanism for)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:143444 CAPLUS
DOCUMENT NUMBER: 114:143444
TITLE: Preparation of 1-aryl-4-carboxyalkylpiperazines and
related compounds as serotoninergic antagonists
INVENTOR(S): Cliffe, Ian Anthony
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., UK
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 395312	A2	19901031	EP 1990-304250	19900420
EP 395312	A3	19910508		
EP 395312	B1	19990512		
R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE				
CA 2015034	AA	19901022	CA 1990-2015034	1990042D
AU 9053779	A1	19901025	AU 1990-53779	19900420
AU 619678	B2	19920130		
GB 2230781	A1	19901031	GB 1990-8925	19900420
GB 2230781	B2	19930428		
HU 54666	A2	19910328	HU 1990-2504	19900420
DD 296921	A5	19911219	DD 1990-339954	19900420
ZA 9003019	A	19911224	ZA 1990-3019	19900420
ZA 9003020	A	19911224	ZA 1990-3020	19900420
DD 297968	A5	19920130	DD 1990-339955	19900420
IL 94151	A1	19950831	IL 1990-94151	19900420
AT 179973	E	19990515	AT 1990-304250	19900420
ES 2130116	T3	19990701	ES 1990-304250	19900420
JP 03011059	A2	19910118	JP 1990-106299	19900421
JP 3036786	B2	20000424		
US 5364849	A	19941115	US 1992-911996	19920710
GB 2255976	A1	19921125	GB 1992-15425	19920720
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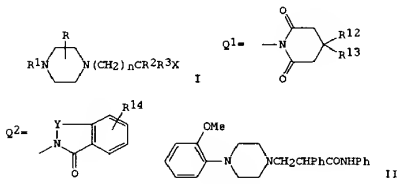
US 5382583	A	19950117	US 1992-998887	19921229
US 5340812	A	19940823	US 1993-1428	19930107
US 5420278	A	19950530	US 1994-248124	19940524
US 5541326	A	19960730	US 1994-339000	19941114

PRIORITY APPLN. INFO.:
GB 1989-9209 A 19890422
GB 1989-24323 A 19891028
US 1990-511150 B2 19900419
GB 1990-8925 A3 19900420
US 1991-748496 B1 19910822
US 1991-748497 B1 19910822
US 1991-756932 B1 19910909
US 1992-911996 A3 19920710
US 1992-998887 A3 19921229

OTHER SOURCE(S): MARPAT 114:143444
GI

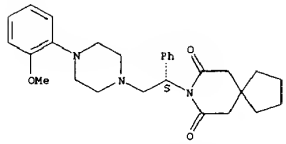
L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. [I; R = H, alkyl; R1 = aryl, N-contg. heteroaryl; R2 =
H, alkyl; R3 = aryl, alkyl, arylalkyl; X = O2CR10, CO2R6, CONR5R9, OCO2R6,
NR4COR6, Q1, Q2, etc.; R4 = H, alkyl; R6 = alkyl, cycloalkyl, arylalkyl;
R9 = H, alkyl, cycloalkyl, aryl, arylalkyl, 8-azaspiro[4.5]deca-7,9-dione-
8-yl-alkyl, etc.; R12, R13 = alkyl; R12R13C = cycloalkyl; R14 = H, halo,
alkyl, alkoxy; Y = CO, SO2; n = 1, 2] were prepd. Thus,
1-(2-methoxyphenyl)piperazine was refluxed 18 h with atropic acid in EtOH
to give .alpha.-[1-[4-(2-methoxyphenyl)piperazinyl]methyl]benzeneacetic
acid. The latter in CH2Cl2 was treated with carbonyldiimidazole and then
aniline to give title compd. II. I bound to rat hippocampal 5-HT1A
receptors with IC50's of 8-127 nM.
IT **132708-63-5P 132709-11-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic antagonist)
RN 132708-63-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-phenylethyl]-, (S)- (9CI) (CA INDEX NAME)

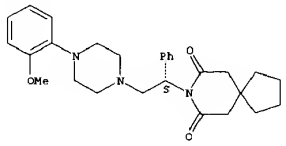
Absolute stereochemistry.

L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 132709-11-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione,
8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-
1-phenylethyl]-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L14 ANSWER 187 OF 263 CAPLUS COPYRIGHT 2002 ACS

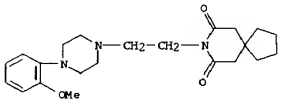
ACCESSION NUMBER: 1991:136585 CAPLUS
DOCUMENT NUMBER: 114:136585
TITLE: The effect of putative 5-HT1A receptor antagonists on
8-OH-DPAT-induced hypothermia in rats and mice
AUTHOR(S): Moser, Paul C.
CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, F-67009, Fr.
SOURCE: Eur. J. Pharmacol. (1991), 193(2), 165-72
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of 3 putative 5-HT1A receptor antagonists (NAN-190, BMY 7378, and WB 4101) were studied on the hypothermia induced by 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT). In order to control for the .alpha.1-adrenoceptor antagonist activity of NAN-190 and WB 4101, the effects of prazosin were also examd. Both NAN-190 and WB 4101 lowered body temp. in the mouse. This effect appeared to be due to their .alpha.1-adrenoceptor antagonist effects, as prazosin had a similar profile. Neither NAN-190, WB 4101 nor prazosin antagonized the hypothermic effects of 8-OH-DPAT. BMY 7378 slightly lowered body temp. but to a lesser extent than 8-OH-DPAT and, in contrast to the other compds. studied, also prevented a fall in body temp. on injection of 8-OH-DPAT. In the rat there was much less interference from .alpha.1-adrenoceptor antagonist activity as both NAN-190 and prazosin only slightly reduced body temp. In this species, however, NAN-190 showed marked antagonist activity against 8-OH-DPAT hypothermia. This was not due to .alpha.1-adrenoceptor antagonist activity as prazosin had no effect. In the rat, as in the mouse, BMY 7378 had a partial agonist profile, whereas WB 4101 behaved essentially as an agonist. These results suggest that NAN-190 is a pure antagonist of 8-OH-DPAT-induced hypothermia in rats and that BMY 7378 and WB 4101 are, resp., a partial agonist and an agonist in this test. The rat seems to be the better species for the study of 5-HT1A receptors using 8-OH-DPAT-induced hypothermia as it is less affected by .alpha.1-adrenoceptor antagonist activity and because the mouse model fails to demonstrate an interaction of NAN-190 with 5-HT1A receptors.

IT **21102-95-4**, BMY7378
RL: BIOL (Biological study)
(hydroxydipropylaminotetralin redn. in body temp. response to, serotonin receptor subtype and species in relation to)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 187 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 188 OF 263 CAPLUS COPYRIGHT 2002 ACS

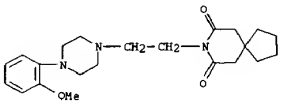
ACCESSION NUMBER: 1991:136473 CAPLUS
DOCUMENT NUMBER: 114:136473
TITLE: Agonist action at 5-HT1C receptors facilitates 5-HT1A receptor-mediated spontaneous tail-flicks in the rat
AUTHOR(S): Bervoets, Karin; Millan, Mark J.; Colpaert, Francis C.
CORPORATE SOURCE: Neurobiol. Div., FONDAX, Puteaux, 92800, Fr.
SOURCE: Eur. J. Pharmacol. (1990), 191(2), 185-95
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In rats lightly restrained in plastic cylinders, s.c. administration of the selective, high-efficacy 5-HT1A receptor agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT) induced spontaneous tail flicks. The putative 5-HT1B receptor agonist CGS 12066B, the mixed 5-HT1B/1C receptor agonists 1-[3-(trifluoromethyl)phenylpiperazine (TFMPP) and 1-(3-chlorophenyl)piperazine (mCPP), the 5-HT1C/2 receptor agonist ((.+-.)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI), and the 5-HT1B/1C/2 receptor agonist quipazine did not elicit tail flicks when applied alone. However, TFMPP, mCPP, DOI, and quipazine, but not CGS 12066B, each potentiated the action of 8-OH-DPAT. Further, in the presence of TFMPP, mCPP, and DOI, the dose-receptor curve for the induction of tail flicks by 8-OH-DPAT was both steeper and shifted to the left. Tail flicks induced by another high-efficacy 5-HT1A receptor agonist, lisuride, were also enhanced by TFMPP, mCPP, and DOI. The 5-HT1A receptor partial agonists buspirone and (.+-.)-flesinoxan evoked tail-flicks only in the presence of TFMPP, mCPP, or DOI. The mixed 5-HT1C/2 receptor antagonists ritanserin and ICI 169,369 did not modify the action of 8-OH-DPAT alone but abolished the potentiation of 8-OH-DPAT-induced tail flicks by DOI and TFMPP. Further, the selective 5-HT1A receptor antagonist BMY 7378 blocked tail flicks induced by both 8-OH-DPAT alone and 8-OH-DPAT plus DOI or TFMPP. A common property of those drugs potentiating 8-OH-DPAT-induced tail flicks is an agonist action at 5-HT1C receptors and the data indicate that it is this mechanism which underlies the facilitation of tail flicks.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(behavior induced by 5-HT1A and 5-HT1C receptor agonist inhibition by)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 188 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:36477 CAPLUS
DOCUMENT NUMBER: 114:36477
TITLE: Functional characterization of neuronal pre- and postsynaptic .alpha.2-adrenoceptor subtypes in guinea pig submucosal plexus
AUTHOR(S): Shen, K. Z.; Barajas-Lopez, C.; Surprenant, A.
CORPORATE SOURCE: Vollum Inst., Oregon Health Sci. Univ., Portland, OR, 97201, USA
SOURCE: Br. J. Pharmacol. (1990), 101(4), 925-31
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

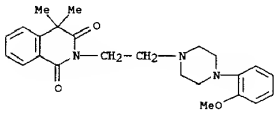
AB The .alpha.2-adrenoceptors on cell bodies of submucosal neurons, on presynaptic cholinergic nerve terminals innervating submucosal neurons, and on presynaptic sympathetic fibers innervating submucosal arterioles were characterized in functional studies by use of subtype selective ligands. Both membrane hyperpolarization and presynaptic inhibition of nicotinic excitatory synaptic potentials (e.p.s.ps) produced by UK 14304 were similarly antagonized by idazoxan, yohimbine, SKF 104078, WB 4101, and ARC 239. Antagonism was competitive and dissocn. equil. consts. were the same for both effects. Vasoconstriction of submucosal arterioles in response to stimulation of the sympathetic nerves (20 Hz for 2 s) was inhibited by UK 14304 and clonidine; concns. producing half-max. responses were 6 and 10 nM, resp. Idazoxan, yohimbine, WB 4101, and SKF 104078 antagonized this action, with dissocn. consts. similar to those for antagonism of the postsynaptic membrane hyperpolarization and presynaptic inhibition of nicotinic e.p.s.ps. Oxymetazoline was a partial agonist when membrane hyperpolarization or presynaptic inhibition of nicotinic e.p.s.ps were measured but a full agonist when presynaptic inhibition of sympathetically-mediated arteriolar vasoconstriction was measured. As an agonist, oxymetazoline produced half-max. responses at 80-120 nM; the dissocn. const. for oxymetazoline as an antagonist was 130 nM. Neither prazosin nor chlorpromazine (up to 30 .mu.M) altered any of the 3 responses to .alpha.2-adrenoceptor agonists. Thus, .alpha.2-adrenoceptors present on submucosal neuronal cell bodies, on presynaptic cholinergic nerve terminals, and on presynaptic sympathetic nerve terminals are the .alpha.2A subtype. However, functional characterization of this subtype differs from that provided by ligand binding studies.

IT **67339-62-2**, ARC 239

L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RL: BIOL (Biological study)
(.alpha.2-adrenoceptor mediated submucosal plexus activity stimulation by UK 14304 inhibition by)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS

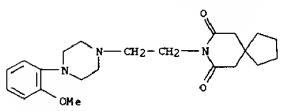
ACCESSION NUMBER: 1991:35858 CAPLUS
DOCUMENT NUMBER: 114:35858
TITLE: Behavioral effects of serotonin agonists and antagonists in the rat and marmoset
AUTHOR(S): Elliott, P. J.; Walsh, D. M.; Close, S. P.; Higgins, G. A.; Hayes, A. G.
CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Herts., SG12 0DP, UK
SOURCE: Neuropharmacology (1990), 29(10), 949-56
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was conducted to investigate the effects of various 5-HT agonists and antagonists on motor behavior in rats and marmosets. Various motor-based responses were assessed after central or peripheral administration of 5-HT agents to rats and marmosets. Drugs acting as agonists at the 5-HT1A receptor (8-OHDPAT, gepirone, BMY-7378, NAN-190, PAPP (LY165163) and flesinoxan) and 5-HT2/1C receptors (DOI) were found to reverse neuroleptic-induced catalepsy in the rat, whereas 5-HT2/1C antagonists (mianserin, ritanserin and ICI-170,809) and the 5-HT1 antagonist ((.+-.)pindolol) increased catalepsy. Agonists acting at 5-HT3 receptors (phenylbiguanide and 2-methyl-5-HT) had no effect on catalepsy. The putative 5-HT1A antagonist, (.+-.)-pindolol, attenuated the reversal of catalepsy by 8-OHDPAT. Although both 8-OHDPAT and BMY-7378 were tested, only the latter was found to reduce apomorphine-induced stereotypy. Bilateral or unilateral infusions of 8-OHDPAT, BMY-7378 or pindolol into the substantia nigra of non-lesioned rats had no effect on spontaneous locomotor or rotational activity, resp. However, 8-OHDPAT and BMY-7378 were found to increase or decrease motor activity, after injection into the median or dorsal raphe nuclei, resp. Finally, 8-OHDPAT and BMY-7378 were found to be inactive against MPTP-induced bradykinesia in the marmoset. It is concluded that both 5-HT1A and 5-HT2/1C receptors are involved in the anti-cataleptic effects of 5-HT agents. The 5-HT1A receptors are probably situated within the raphe, whereas the location of the 5-HT2/1C receptors remains undetd.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(behavior response to, brain serotoninergic receptors in)

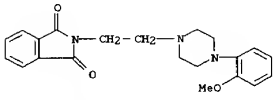
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

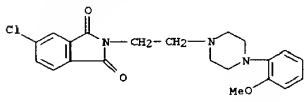


●2 HCl

L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



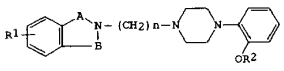
RN 130976-13-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 5-chloro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:12226 CAPLUS
DOCUMENT NUMBER: 114:12226
TITLE: Preparation of N,N'-disubstituted piperazines for treatment of dysuria
INVENTOR(S): Hachisu, Mitsugi; Yoshida, Seishi; Takahashi, Hiroko; Ishii, Yuko; Tsuruoka, Takashi; Inoue, Shigeharu
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

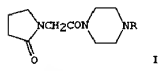
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02184667	A2	19900719	JP 1989-5482	19890111

OTHER SOURCE(S): MARPAT 114:12226
GI

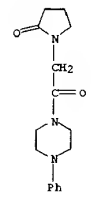


AB Pharmaceuticals for treatment of dysuria contain the title compds. I (A = CH2, CO; B = CO, SO2; R1 = H, halo; R2 = Cl-3 alkyl; n = 2-4) or their pharmacol. acceptable salts as active ingredients. The treatment of 1-(2-methoxyphenyl)piperazine with 2-(2-bromoethyl)phthalimidine and Na2CO3 in DMF at room temp. for 16 h gave 73% 2-[4-(2-methoxyphenyl)piperazinoethyl]phthalimidine (II), which blocked .alpha.1-adrenaline receptor in aorta and urethra with pA2 of 8.1 and 8.2, resp., vs. 8.6 and 8.1, for the control contg. prazosin, resp. Tablets were formulated contg. II 10.0, lactose 86.8, corn starch 37.0, poly(vinylpyrrolidone) 5.0, and Mg stearate 1.2 mg.
IT **99718-67-9P 130976-13-5P**
RL: PREP (Preparation)
(prepn. of, for treatment of dysuria)
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

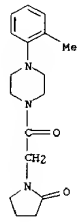
L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:6443 CAPLUS
DOCUMENT NUMBER: 114:6443
TITLE: Potential nootropic agents: synthesis of a series of (2-oxo-1-pyrrolidinyl)acetic acid piperazides
AUTHOR(S): Valenta, Vladimir; Sindelar, Karel; Holubek, Jiri; Ryska, Miroslav; Krejci, Ivan; Dlabac, Antonin; Protiva, Miroslav
CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.
SOURCE: Collect. Czech. Chem. Commun. (1990), 55(6), 1613-29
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:6443
GI



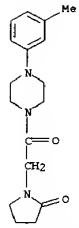
AB The title compds., e.g., I (R = Me, CH2CH2OMe, CH2Ph, CO2Et, Ph, substituted Ph) were prepd. by heating Et (2-oxo-1-pyrrolidinyl)acetate with a series of N-monosubstituted piperazines. The propionamides' e.g., I (CH2CH2CONH2), were obtained by reactions of the acid chlorides with 3-(1-piperazinyl)propionamide. I (R = Me, CH2CH2OMe) proved more active than piracetam by their antiamnesic effects in rats, by antagonizing the brain-damaging effects of cycloheximide in infantile rats, and by their potentiation of the effects of anticonvulsant agents.
IT **131027-95-7P 131027-96-8P 131027-97-9P**
131027-98-0P 131027-99-1P 131028-00-7P
131028-01-8P 131028-02-9P 131028-23-4P
131028-24-5P 131028-25-6P 131028-26-7P
131028-27-8P 131028-28-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 131027-95-7 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



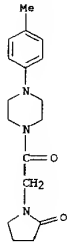
RN 131027-96-8 CAPLUS
CN Piperazine, 1-(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-
(9CI)
(CA INDEX NAME)



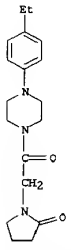
RN 131027-97-9 CAPLUS
CN Piperazine, 1-(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-
(9CI)
(CA INDEX NAME)



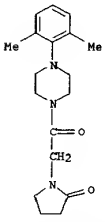
RN 131027-98-0 CAPLUS
CN Piperazine, 1-(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)



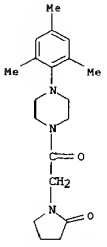
RN 131027-99-1 CAPLUS
CN Piperazine, 1-(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA
INDEX NAME)



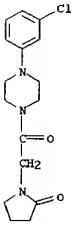
RN 131028-00-7 CAPLUS
CN Piperazine, 1-(2,6-dimethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-
(9CI)
(CA INDEX NAME)



RN 131028-01-8 CAPLUS
CN Piperazine,
1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-(2,4,6-trimethylphenyl)-
(9CI) (CA INDEX NAME)

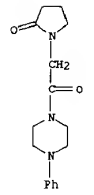


RN 131028-02-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)



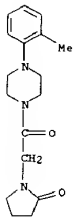
RN 131028-23-4 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl-,
monohydrochloride
(9CI) (CA INDEX NAME)

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

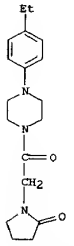
RN 131028-24-5 CAPLUS
CN Piperazine, 1-(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

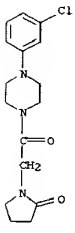
RN 131028-25-6 CAPLUS
CN Piperazine, 1-(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



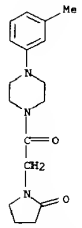
● HCl

RN 131028-28-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



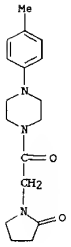
● HCl

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 131028-26-7 CAPLUS
CN Piperazine, 1-(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 131028-27-8 CAPLUS
CN Piperazine, 1-(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

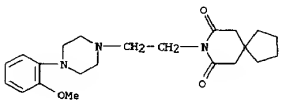
L14 ANSWER 193 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:604753 CAPLUS
DOCUMENT NUMBER: 113:204753
TITLE: 5-HT1A agonist effects on punished responding of squirrel monkeys
AUTHOR(S): Gleeson, S.; Barrett, J. E.
CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20889-4799, USA
SOURCE: Pharmacol., Biochem. Behav. (1990), 37(2), 335-7
CODEN: PBBHAU; ISSN: 0091-3057
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Buspirone and other drugs that act as 5-HT1A agonists appear to be clin. effective anxiolytics in humans, yet their anticonflict effects, though robust in pigeons, are equivocal in rodents. In the present study the effects of the benzodiazepine midazolam and a series of 5-HT1A agonists were examd. on punished responding of squirrel monkeys. Lever presses were reinforced according to a fixed-interval 3-min schedule; in addn., each 30th lever press was punished. Midazolam produced large increases in response rates, whereas none of the 5-HT1A compds. produced any increases in responding. Most of these drugs decreased response rates at the higher doses examd. Although the reasons for the discrepancy between species in the anticonflict effects of serotonergic anxiolytics cannot be specified, the different anatomical distribution of 5-HT1A binding sites across species may suggest a different functional role for this receptor.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(punished behavior response to, in squirrel monkeys)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

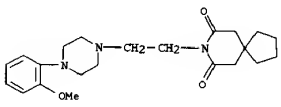


●2 HCl

L14 ANSWER 193 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:471240 CAPLUS
DOCUMENT NUMBER: 113:71240
TITLE: BMY 7378: partial agonist at spinal cord 5-HT1A receptors
AUTHOR(S): Zemlan, Frank P.; Zieleniewski-Murphy, Anne; Murphy, R. Maureen; Behbehani, Michael M.
CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, 45267-0559, USA
SOURCE: Neurochem. Int. (1990), 16(4), 515-22
CODEN: NEUIDS; ISSN: 0197-0186
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent data indicate that BMY 7378 demonstrates high affinity, selectivity and low intrinsic activity at hippocampal 5-HT1A receptors, suggesting that BMY 7378 may represent the first selective 5-HT1A functional antagonist. The present study examd. the agonist and antagonist properties of BMY 7378 at spinal cord 5-HT1A receptors. In electrophysiol. studies, iontophoretic administration of either the 5-HT1A agonist 8-OH-DPAT (43.8 nA) or BMY 7378 (46.3 nA) significantly inhibited the firing rate of wide-dynamic-range dorsal horn units indicating that BMY 7378 demonstrates significant intrinsic activity at spinal cord 5-HT1A receptors. Concomitant BMY 7378 and 8-OH-DPAT administration identified no BMY 7378 ejection current (20-100 nA) which antagonized the 8-OH-DPAT induced inhibition of dorsal horn unit activity. In behavioral studies in the spinal rat, 8-OH-DPAT increased the animals' sensitivity to noxious levels of mech. stimulation (ED50 = 269 nmol/kg) as did BMY 7378 (ED5) = 295 nmol/kg) with no statistically significant differences in the maximal response (Ymax) obsd. Concomitant BMY 7378 and 8-OH-DPAT administration identified no BMY 7378 dose (10-1100 nmol/kg) which blocked the hyperalgesic effect of 8-OH-DPAT, rather, each drug produced similar effects which were additive. Further, the 5-HT1A-agonist effects of BMY 7378 were blocked by the 5-HT1A antagonist spiperone. Therefore, both the electrophysiol. and reflex data indicate that BMY 7378 possesses intrinsic activity at spinal cord 5-HT1A receptors, and like 8-OH-DPAT is a partial agonist at these receptors. Differences in BMY 7378 intrinsic activity at spinal cord as opposed to hippocampal 5-HT1A receptors are discussed in terms of regional differences in G-proteins coupled to 5-HT1A receptors in

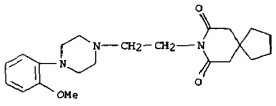
L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
these two CNS regions.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(as serotoninergic S1A receptor partial antagonist, in spinal cord)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 195 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:471154 CAPLUS
DOCUMENT NUMBER: 113:71154
TITLE: RU 24969-induced emesis in the cat: 5-HT1 sites other than 5-HT1A, 5-HT1B or 5-HT1C implicated
AUTHOR(S): Lucot, James B.
CORPORATE SOURCE: Dep. Pharmacol., Wright State Univ., Dayton, OH, 45435, USA
SOURCE: Eur. J. Pharmacol. (1990), 180(2-3), 193-9
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB RU 24969 was administered s.c. to cats and found to elicit with a maximally ED of 1.0 mg/kg. 5-Methoxytryptamine was found to have lower efficacy and to produce a higher incidence of non-specific effects while trifluoromethylphenylpiperizine was devoid of emetic effects. The emesis elicited by 1.0 mg/kg of RU 24969 was not altered by pretreatment with phentolamine, haloperidol, yohimbine or (-)-propranolol, indicating that catecholamines played no role in this response. The emesis was prevented by metergoline and methylsergide but not by ketanserin, cyproheptadine, mesulergine, ICS 205,930, methiothepin, trimethobenzamide or BMY 7378. An indirect argument is presented that implicates a role for 5-HT1D sites. This conclusion must remain tentative until drugs selective for this site are synthesized and tested. The emesis was also prevented by 8-hydroxy-2-(di-n-propylamine)tetralin, confirming that this drug has a general antiemetic effect in cats.
IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(RU 24969-induced emesis response to, serotonin receptor sites in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

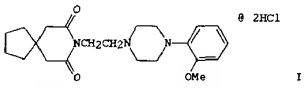
L14 ANSWER 195 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:191749 CAPLUS
DOCUMENT NUMBER: 112:191749
TITLE: Further investigation of the in vivo pharmacological properties of the putative 5-HT1A antagonist, BMY 7378
AUTHOR(S): Sharp, Trevor; Backus, Lisa I.; Hjorth, Stephan; Bramwell, Steven R.; Grahame-Smith, David G.
CORPORATE SOURCE: Dep. Clin. Pharmacol., Radcliffe Infirm., Oxford, OX2 6HE, UK
SOURCE: Eur. J. Pharmacol. (1990), 176(3), 331-40
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



@ 2HCl

I

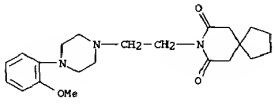
AB The present study examd. the action of the putative 5-HT1A antagonist, BMY 7378 (I) on central pre- and postsynaptic 5-HT1A function in the rat in vivo. Unlike the direct acting 5-HT1A agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT), BMY 7378 (0.25-5 mg/kg s.c.) did not induce the full postsynaptically mediated 5-HT behavioral syndrome (forepaw treading, head weaving, flat body posture, hindlimb abduction). Indeed, the maximal 5-HT behavioral syndrome scores for BMY 7378 were about 10% of those for 8-OH-DPAT. Following pretreatment, however, BMY 7378 concn.-dependently (0.25-5 mg/kg s.c.) reduced to undetectable levels forepaw treading and head weaving induced by 8-OH-DPAT (0.75 mg/kg s.c.). BMY 7378 also inhibited stereotypy and locomotor activity induced by 0.5 mg/kg apomorphine at 5 mg/kg. In contrast to its apparent 5-HT1A antagonist properties in the behavioral expts., BMY 7378 caused a marked and concn.-dependent (0.01-1.0 mg/kg s.c.) decrease of 5-HT release in ventral hippocampus of the anesthetized rats as detected by brain microdialysis. This effect of BMY 7378 had a similar onset and duration of action but with slightly reduced efficacy compared to that previously described for 8-OH-DPAT. As with 8-OH-DPAT, the inhibitory effect of BMY

L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

7378 on 5-HT release was attenuated by pretreatment with the 5-HT1 receptor/.beta.-adrenoceptor antagonist pindolol (8 mg/kg s.c.) but not its counterpart propranolol (20 mg/kg s.c.). Pretreatment with a combination of the .beta.1- and .beta.2-adrenoceptor antagonists metoprolol (4 mg/kg s.c.) and ICI 118551 (4 mg/kg s.c.), resp., did not alter the 5-HT response to BMY 7378. BMY 7378 is a mixed agonist/antagonist at central 5-HT1A receptors.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotoninergic S1A receptors of brain response to, mixed agonist-antagonist activity in relation to)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



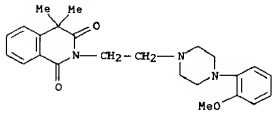
●2 HCl

L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS

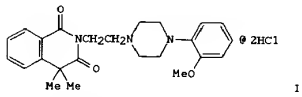
ACCESSION NUMBER: 1990:152352 CAPLUS
DOCUMENT NUMBER: 112:152352
TITLE: Subtypes of .alpha.1-adrenoceptors in hippocampus of pigs, guinea pigs, calves and humans: regional differences
AUTHOR(S): Hoyer, Daniel; Jones, C. Richard; Ford, William; Palacios, Jose M.
CORPORATE SOURCE: Preclin. Res., Sandoz Ltd., Basel, CH-4002, Switz.
SOURCE: Eur. J. Pharmacol., Mol. Pharmacol. Sect. (1990), 188(1), 9-16
CODEN: EJPPET; ISSN: 0922-4106
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radioligand binding studies were performed with membranes of guinea-pig, pig, calf, and human hippocampus using [125I]-labeled BE 2254 (also known as [125I]-labeled HEAT as the radioligand. [125I]-labeled BE 2254 bound with similar high affinity to saturable populations of recognition sites in all 4 membrane prepns. Competition curves obtained with a variety of ligands (e.g., WB 4101, benoxathian, 5-methyl-urapidil) were biphasic and the profiles of the high- and low-affinity components of [125I]-labeled BE 2254 binding were similar in all four membrane prepns. The data suggest that [125I]-labeled BE 2254 labels 2 subtypes of .alpha.1-adrenoceptors in the hippocampus of these species. [3H]WB 4101 was used to label .alpha.1A recognition sites in pig hippocampus membranes. [3H]WB 4101 recognized with high affinity an apparently homogeneous class of sites, as suggested by monophasic satn. and competition expts. The rank order of affinity of the compds. for the high-affinity component of [125I]-labeled BE 2254 binding was similar to the rank order of affinity of these drugs for [3H]WB 4101 sites. The pharmacol. profile of the low-affinity component of [125I]-labeled BE 2254 binding was similar to that described recently for the .alpha.1B-adrenoceptor cloned from DDT1 cells. In autoradiog. studies with human hippocampal slices, CEC (chloroethylclonidine), an alkylating agent described to show selectivity for .alpha.1B-adrenoceptors, displaced preferentially [125I]-labeled BE 2254 binding from the mol. layer of the dentate gyrus. In contrast, WB 4101 an .alpha.1A-adrenoceptor-selective ligand, displaced preferentially [125I]-labeled BE 2254 binding in the hilus and the CA3 region. The data show that 2 subtypes of .alpha.1-adrenergic recognition sites can be identified in the hippocampus. In the human hippocampus, .alpha.1A sites

L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
are predominant in the hilus and the CA3 region, whereas .alpha.1B sites
are predominant in the mol. layer of the dentate gyrus. These subtypes
show a similar pharmacol. profile in man, pig, calf and guinea-pig, and
may have a different functional role in these two areas of the hippocampus.
IT **67339-62-2**, ARC 239
RL: BIOL (Biological study)
(.alpha.1 adrenoceptor subtypes affinity for, of hippocampus of human
and lab. animal)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

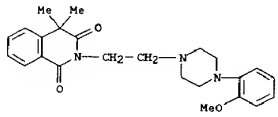


L14 ANSWER 198 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:62442 CAPLUS
DOCUMENT NUMBER: 112:62442
TITLE: Infrared spectroscopy study of interactions affecting
tablet disintegration and drug release rate
AUTHOR(S): Casahoursat, L.; Pham Van Huong; Larrouture, D.; Heraud, P.; Etienne, A.
CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.
SOURCE: Pharm. Acta Helv. (1989), 64(8), 225-30
CODEN: PAHEAA; ISSN: 0031-6865
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



I

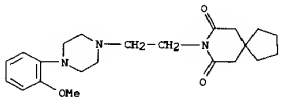
AB IR spectroscopy studies showed that the interaction between the drug (e.g., ARC.2HCL) (I) and excipients necessary for tablet formulations affected the drug release rate. The interaction was higher at higher compression pressures.
IT **55974-42-0**
RL: PRP (Properties)
(interaction of, with excipients, IR spectroscopy study of)
RN 55974-42-0 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:587459 CAPLUS
DOCUMENT NUMBER: 111:187459
TITLE: Behavioral studies with anxiolytic drugs. VI. Effects on punished responding of drugs interacting
with serotonin receptor subtypes
AUTHOR(S): Gleeson, S.; Ahlers, S. T.; Mansbach, R. S.; Foust, J.
M.; Barrett, J. E.
CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci.,
Bethesda, MD, 20814-4799, USA
SOURCE: J. Pharmacol. Exp. Ther. (1989), 250(3), 809-17
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of drugs that bind selectively to different 5-HT receptor subtypes were assessed in pigeons. Keypecking was maintained by a multiple fixed-ratio schedule of reinforcement in which responding also
was punished during one component. The greatest increases in punished
responding were produced by the buspirone analogs BMY 7378 and ipsapirone,
which act at the 5-HT1A receptor. RU 24969, with high affinity for both
5-HT1A and 5-HT1B receptors, and 1-(2-methoxyphenyl)piperazine, a 5-HT1
compd., increased punished responding to a lesser extent, as did the 5-HT2
antagonists ketanserin and ritanserin. The 5-HT3 antagonists GR 38032F,
ICS 205930, and MDL 72222 showed little systematic effect, and the mixed
5-HT1B/5-HT1C compd. 1-(3-chlorophenyl)piperazine decreased punished
responding. Levels of neurotransmitter metabolites in cerebrospinal fluid
were assessed across a wide dose range of representative drugs used in the
behavioral studies. Levels of the 5-HT metabolite 5-HIAA were decreased
by BMY 7378 and ipsapirone, were not changed by ritanserin, and were
increased at one dose by MDL 72222. Thus, decreased 5-HT neurotransmission is involved in the effects of novel nonbenzodiazepine
anxiolytics such as buspirone. The effects of these drugs on other neurotransmitter systems do not play a significant role in their anxiolytic actions.
IT **21102-95-4**, BMY 7378
RL: PRP (Properties)
(behavioral anxiolytic effect of, serotonin receptor subtypes in, cerebrospinal fluid monoamine metabolites response to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

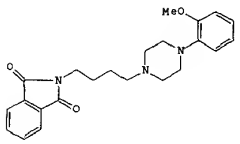
L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:205083 CAPLUS
DOCUMENT NUMBER: 110:205083
TITLE: Stimulus properties of Arylpiperazines: NAN-190, a potential 5-HT1A serotonin antagonist
AUTHOR(S): Glennon, R. A.; Naiman, N. A.; Pierson, M. E.; Titeler, M.; Lyon, R. A.; Herndon, J. L.; Misenheimer, B.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298-0581, USA
SOURCE: Drug Dev. Res. (1989), 16(2-3-4), 335-43
CODEN: DDREDK; ISSN: 0272-4391
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



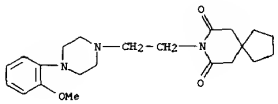
I

AB Arylpiperazines bind both at 5-HT1A and 5-HT1B serotonin receptors. In an attempt to design novel 5-HT1A agonists and antagonists based on the arylpiperazine nucleus, the stimulus properties of a series of such agents were studied in rats trained to discriminate 0.5 mg/kg of the 5-HT1B activity. The agents were modified to eliminate those features and to incorporate structural features important for the 5-HT1A activity. The resulting agents displayed high affinity for 5-HT1A sites. NAN-190 I neither mimicked nor antagonized the TFMPP stimulus, but was capable of antagonizing the stimulus produced by the 5-HT1A agonist 8-hydroxy-2-(dipropylamino)tetralin (0.2 mg/kg). NAN-190 may be a potential 5-HT1A antagonist.

IT **21102-95-4**, BMY 7378
RL: BIOL (Biological study)
(serotonin receptors interaction with, structure in relation to)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

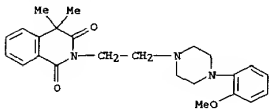
L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:101584 CAPLUS
DOCUMENT NUMBER: 110:101584
TITLE: Demonstration by infrared spectroscopy of the interactions affecting disintegration time of tablets and drug release rate
AUTHOR(S): Casahoursat, L.; Pham V. Huong; Larrouture, D.; Heraud, P.; Etienne, A.
CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.
SOURCE: Bull. Tech./Gattefosse Rep. (1987), 80, 33-40
CODEN: BTGRDQ
DOCUMENT TYPE: Journal
LANGUAGE: French

AB IR spectroscopy showed that the interaction between a drug [e.g. AR-C 239-2HCl (I)] and various excipients required for tablet formulation affected the disintegration time of tablets, but not the drug dissoln. rate. The excipients used were lactose, corn starch, gelatin, Mg stearate and poly(vinylpyrrolidone). The dissoln. rate of AR-C-HCl was not affected by the compression force, while that of I decreased with an increase in the compression force. The IR method was superior to the DSC method currently used.

IT **55974-42-0 86891-00-1**
RL: BIOL (Biological study)
(tablets, disintegration of and drug release rate from, excipient interactions effect on, IR spectroscopy study of)

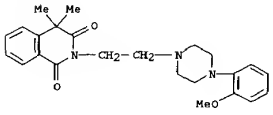
RN 55974-42-0 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

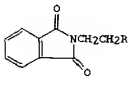
RN 86891-00-1 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:18097 CAPLUS
DOCUMENT NUMBER: 110:18097
TITLE: Antipsychotic properties of new N-(4-substituted-1-piperazinylethyl)- and N-(4-substituted-1-piperidinylethyl)-phthalimides
AUTHOR(S): Al-Rashood, Khalid A.; Mustafa, Ali A.; Alhaider, Abdulqader; Ginawi, Omer T.; Madani, Abdul Azim E.; El-Obeid, Humeida A.
CORPORATE SOURCE: Coll. Pharm., King Saud Univ., Riyadh, 11451, Saudi Arabia
SOURCE: J. Pharm. Sci. (1988), 77(10), 898-901
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



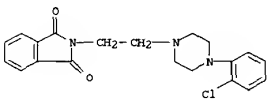
I

AB A series of N-(4-phenyl- and 4-pyridyl-1-piperazinylethyl)- and N-(4-phenyl-1-piperidinylethyl)-phthalimides I (R = 4-aryl-substituted piperazine and piperidine) were synthesized and tested for antipsychotic activity. All compds. suppressed the spontaneous motor activity and the apomorphine-induced climbing in mice and pergolide-induced locomotor activity in rats, demonstrating psychotropic properties equal to the that of sulpiride. Although the compds., like sulpiride, were less potent than haloperidol in blocking the locomotor activities, they caused no catalepsy, a major side effect following treatment with conventional antipsychotic agents. It is likely that the new compds. produce their neuroleptic activities through inhibition of limbic dopamine receptors.

IT **75000-28-1P 75000-29-2P 75000-30-5P 117992-67-3P 117992-68-4P 117992-69-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antipsychotic activity of)

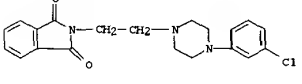
RN 75000-28-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-

L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



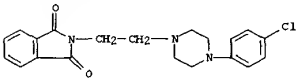
● HCl

RN 117992-68-4 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



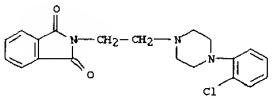
● HCl

RN 117992-69-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

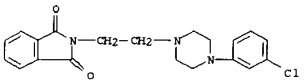


● HCl

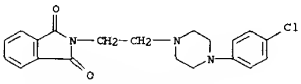
L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(9CI) (CA INDEX NAME)



RN 75000-29-2 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



RN 75000-30-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



RN 117992-67-3 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:590450 CAPLUS
DOCUMENT NUMBER: 109:190450
TITLE: Preparation of pyridazinone-containing piperazine derivatives and their salts as cardiotonics
INVENTOR(S): Okujima, Hiromi; Narimatsu, Akihiro; Kobayashi, Makio; Furuya, Rikizo; Tsuda, Kunio; Kitada, Yoshi
PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63154671	A2	19880627	JP 1986-300695	19861217

OTHER SOURCE(S): MARPAT 109:190450
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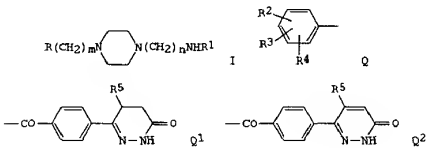
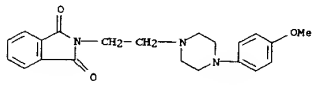


I Q

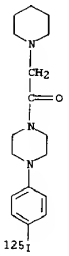
Q1 Q2

AB Title derivs. I (R = Q; R1 = Q1, Q2; R2 - R4 = H, C1-5 alkoxy, OH; R5 = H, C1-5 alkyl; two of R2 - R4 = OCH2O, OCH2CH2O; m = 0-4; n = 1-4) and their salts are prepd. as cardiotonics. A soln. of 1-(4-methoxyphenyl)piperazine and N-(2-bromoethyl)phthalimide in DMF was treated with Et3N at 80.degree. for 5 h and the product (yield 28%) was stirred with an aq. H2NNH2.H2O in EtOH at 70.degree. for 4 h to give 100 % I (R = C6H4OMe-4, R1 = H, m = 0, n = 2) (II). 6-(4-Carboxyphenyl)-2,3,4,5-tetrahydropyridazin-3-one (0.75 g) was treated with ClCO2Et in DMF/THF contg. Et3N between -20 and -30.degree., the reaction mixt. was treated with a soln. of 0.81 g I1 at -20.degree. for 20 min, and then at room temp. for 2 h to give I (R = C6H4OMe-4, R1 = Q1, R5 = H, m = 0, n = 2) (III), which was treated with aq. HCl/EtOH to give 0.85 g II1.HCl (IV). In guinea pig left atrium in vitro, IV at 10-5 or 3 .times. 10-5 g/mL

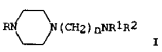
L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
increased cardiac contractility 42.1 or 58.0%, resp.
IT **117046-73-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 117046-73-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



L14 ANSWER 204 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:586395 CAPLUS
DOCUMENT NUMBER: 109:186395
TITLE: The metabolic and kinetic aspects of 1-(piperidinoacetyl)-4-(4-iodophenyl)piperazine: a potential brain imaging agent
AUTHOR(S): Hariharan, Shankar
CORPORATE SOURCE: Northeastern Univ., Boston, MA, USA
SOURCE: (1987) 238 pp. Avail.: Univ. Microfilms Int., Order
No. DA8801974
From: Diss. Abstr. Int. B 1988, 48(11), 3260
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **117205-94-4**, 1-(Piperidinoacetyl)-4-(4-[125I]iodophenyl)piperazine
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, brain imaging in relation to)
RN 117205-94-4 CAPLUS
CN Piperazine, 1-[4-(iodo-125I)phenyl]-4-(1-piperidinylacetyl)- (9CI) (CA
INDEX NAME)

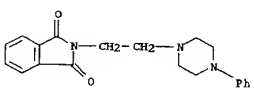


L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:528953 CAPLUS
DOCUMENT NUMBER: 109:128953
TITLE: Arylpiperazine derivatives as high-affinity 5-HT1A serotonin ligands
AUTHOR(S): Glennon, Richard A.; Naiman, Noreen A.; Lyon, Robert A.; Titeler, Milt
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298-0581, USA
SOURCE: J. Med. Chem. (1988), 31(10), 1968-71
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:128953
GI



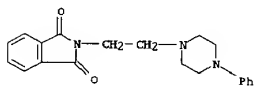
I

AB A small series of 4-substituted 1-arylpiperazines I (R = Ph, 2-MeOC6H4, 1-naphthyl, 2-pyrimidinyl; NR1R2 = phthalimido, NH2, NHAc, NHBz; n = 2-5) was prepd. in an attempt to develop agents with high affinity for 5-HT1A (5-hydroxytryptamine1A) serotonin binding sites. I (R = Ph, 2-MeOC6H4, 1-naphthyl; NR1R2 = phthalimido, NHBz; n = 4) displayed high affinities for these sites. One of these compds., I (R = 2-MeOC6H4, NR1R2 = phthalimido, n = 4), possessed a higher affinity than 5-HT and represents the highest affinity (Ki = 0.6 nM) agent yet reported for 5-HT1A sites.
IT **75000-24-7P 115338-31-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and binding affinity of, for hydroxytryptamine receptor site)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-
(9CI)
(CA INDEX NAME)



L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 115338-31-3 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-,
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS

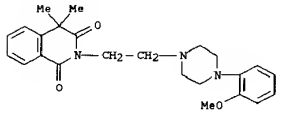
ACCESSION NUMBER: 1988:417541 CAPLUS
DOCUMENT NUMBER: 109:17541
TITLE: Alpha-2A and alpha-2B adrenergic receptor subtypes:
antagonist binding in tissues and cell lines containing only one subtype
AUTHOR(S): Bylund, David B.; Ray-Prenger, Carla; Murphy, T. J.
CORPORATE SOURCE: Sch. Med., Univ. Missouri, Columbia, MO, 65212, USA
SOURCE: J. Pharmacol. Exp. Ther. (1988), 245(2), 600-7
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The affinities of 34 adrenergic antagonists for .alpha.2-adrenergic receptors were detd. from homogenate radioligand binding studies with [3H]yohimbine and [3H]rauwolscine. It has been suggested that .alpha.2-adrenergic receptors can be subdivided into .alpha.2A and .alpha.2B subtypes. Oxymetazoline is selective for .alpha.2A receptors, whereas prazosin is .alpha.2B selective. Five different tissues were used, each of which has only 1 of the 2 subtypes: human platelets (.alpha.2A), the HT29 cell line (.alpha.2A), human cerebral cortex (.alpha.2A), neonatal rat lung (.alpha.2B), and NG108-15 cell line (.alpha.2B). The drug affinities were highly correlated when .alpha.2A tissues were compared with .alpha.2A tissues (r = 0.97-0.98) or when the 2 .alpha.2B tissues were compared (r = 0.99). By contrast, comparison of an .alpha.2A tissue with an .alpha.2B tissue resulted in poor correlations (r = 0.77 to -0.87). Three new subtype-selective drugs were identified among these drugs on the basis of at least a 10-fold greater affinity for 1 subtype. All 3 were selective for the .alpha.2B subtype: ARC-239 (100-fold selective), chlorpromazine (10-fold selective), and 7-hydroxychlorpromazine (17-fold selective). These studies, by demonstrating distinct pharmacol. profiles for the 2 .alpha.2-adrenergic receptor subtypes in several different tissues, further support the existence and definition of these subtypes. The identification of a cell line for each subtype should be useful in the further study of .alpha.2-adrenergic receptor subtypes.

IT **67339-62-2**, ARC 239
RL: BIOL (Biological study)
(as .alpha.2B adrenergic receptor ligand)

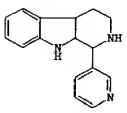
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:568626 CAPLUS
DOCUMENT NUMBER: 107:168626
TITLE: Synthesis and pharmacological properties of some 2-substituted 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-carbolines
AUTHOR(S): Misztal, Stanislaw; Boksa, Jan; Chojnacka-Wojcik, Ewa; Tatarczynska, Ewa; Lewandowska, Anna
CORPORATE SOURCE: Inst. Pharmacol., Pol. Acad. Sci., Krakow, 31-343, Pol.
SOURCE: Pol. J. Pharmacol. Pharm. (1987), 39(1), 97-103
CODEN: PJPPAA; ISSN: 0301-0244
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:168626
GI



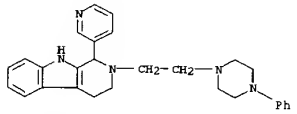
I

AB The title compds. I (R = COCH2NMe2, (CH2)2NMe2, COCH2piperidyl, (CH2)2piperidyl, etc.) were obtained by chloro- or bromoacetylation of 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-carboline followed by reaction with the appropriate amine and LiAlH4 redn. Some of the compds. showed sedative properties in mice. None possessed neuroleptic, antidepressant, analgesic, or anticonvulsant properties.

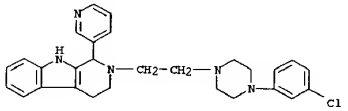
IT **110785-29-0P 110785-30-3P**
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuropharmacol. and toxicity of)

RN 110785-29-0 CAPLUS
CN 1H-Pyrido[3,4-b]indole, 2,3,4,9-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

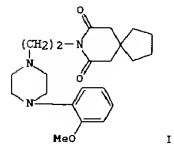


RN 110785-30-3 CAPLUS
CN 1H-Pyrido[3,4-b]indole, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3,4,9-tetrahydro-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:489746 CAPLUS
DOCUMENT NUMBER: 107:89746
TITLE: BMY 7378, a buspirone analog with high affinity, selectivity and low intrinsic activity at the 5-HT1A receptor in rat and guinea pig hippocampal membranes
AUTHOR(S): Yocca, Frank D.; Hyslop, Deborah K.; Smith, David W.; Maayani, Saul
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers Co., Wallingford, CT, 06492-7660, USA
SOURCE: Eur. J. Pharmacol. (1987), 137(2-3), 293-4
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



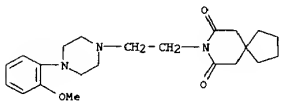
I

AB The buspirone analog BMY7378 (I) had a high affinity and selectivity for 5-HT1A binding sites in rat and guinea pig hippocampal membrane preps.
The drug also had low intrinsic activity.

IT **21102-95-4**
RL: PROC (Process)
(binding of, to serotoninergic S1A receptors of brain)

RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:156511 CAPLUS
DOCUMENT NUMBER: 106:156511
TITLE: Preparation of 3,7-diazabicyclo[3.3.1]nonane-2,4,6,8-tetrone derivatives as central nervous system agents
INVENTOR(S): Schoen, Uwe; Kehrbach, Wolfgang; Benson, Werner; Fuchs, Andreas; Ruhland, Michael
PATENT ASSIGNEE(S): Kali-Chemie Pharma G.m.b.H., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3529872	A1	19870226	DE 1985-3529872	19850821
ES 556660	A1	19871216	ES 1986-556660	19860625
FI 8603150	A	19870222	FI 1986-3150	19860801
FI 82048	B	19900928		
FI 82048	C	19910110		
EP 212551	A2	19870304	EP 1986-111145	19860812
EP 212551	A3	19880323		
EP 212551	B1	19901024		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 57702	E	19901115	AT 1986-111145	19860812
HU 41788	A2	19870528	HU 1986-3603	19860818
HU 194233	B	19880128		
ZA 8606243	A	19870429	ZA 1986-6243	19860819
DD 251555	A5	19871118	DD 1986-293732	19860819
US 4771044	A	19880913	US 1986-898043	19860819
NO 8603346	A	19870223	NO 1986-3346	19860820
NO 164901	B	19900820		
NO 164901	C	19901128		
AU 8661619	A1	19870226	AU 1986-61619	19860820
AU 589671	B2	19891019		
DK 8603961	A	19870430	DK 1986-3961	19860820
DK 161648	B	19910729		
DK 161648	C	19920127		
IL 79785	A1	19900712	IL 1986-79785	19860820
CA 1272196	A1	19900731	CA 1986-516366	19860820
JP 62096489	A2	19870502	JP 1986-194120	19860821
JP 07039416	B4	19950501		
ES 557719	A1	19880101	ES 1987-557719	19870915
JP 07267953	A2	19951017	JP 1994-265587	19941028
JP 2525560	B2	19960821		

PRIORITY APPLN. INFO.: DE 1985-3529872 19850821
EP 1986-111145 19860812

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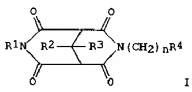
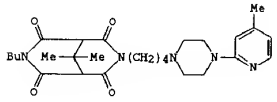
L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



I



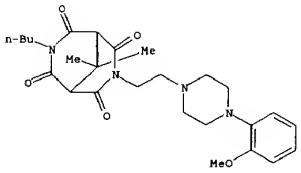
II

AB The title compds. I [R1 = alkyl, alkenyl, cycloalkylalkyl, phenylalkyl; R2, R3 = alkyl, Ph; R2R3 = alkylene; R4 = nucleophilic leaving group, (un)substituted 1-piperazinyl; n = 2-10] were prepd. as central nervous system agents (no data). 3-Butyl-9,9-dimethyl-3,7-diazabicyclo[3.3.1]nonane-2,4,6,8-tetrone was alkylated with Br(CH2)4Br to give I (R1 = Bu, R2 = R3 = Me, R4 = Br, n = 4). This was condensed with 1-(4-methyl-2-pyridinyl)piperazine to give diazabicyclononane II. Tablets, each contg. 20 mg II, were prepd. from II 20, cornstarch 30, lactose 55, polyvinylpyrrolidone 5, Mg stearate 2, and hydrogenated castor oil 1 part.

IT **107736-97-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as central nervous system agent)

RN 107736-97-0 CAPLUS
CN 3,7-Diazabicyclo[3.3.1]nonane-2,4,6,8-tetrone, 3-butyl-7-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-9,9-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



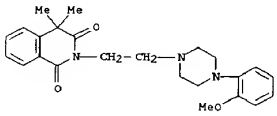
L14 ANSWER 210 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:149183 CAPLUS
DOCUMENT NUMBER: 106:149183
TITLE: The blood pressure effects of alpha-adrenoceptor antagonists injected in the medullary site of action of clonidine: the nucleus reticularis lateralis
AUTHOR(S): Bousquet, Pascal; Feldman, Josiane
CORPORATE SOURCE: Fac. Med., Univ. Louis Pasteur, Strasbourg, 67000, Fr.
SOURCE: Life Sci. (1987), 40(11), 1045-52
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of alpha-blocking drugs were administered to the nucleus reticularis lateralis (NRL) of the medulla oblongata, the main site for the hypotensive action of clonidine, in pentobarbital anesthetized cats. Drugs were injected through a needle which was stereotaxically inserted. Prazosin [19216-56-9] (6 nmol) was hypertensive (MBP (mean blood pressure) = +25%), corynanthine [483-10-3] had no effect and AR-C239 [**67339-62-2**] (7 nmol), another alpha1-blocker, was hypotensive (MBP = -16%). The alpha2-blockers, yohimbine [146-48-5] and idazoxan [79944-58-4] were hypotensive. The blood pressure effects of alpha-blocking drugs directly microinjected in the nucleus reticularis lateralis cannot be simply related to their selectivity for a particular subtype of alpha-receptors.

IT **67339-62-2**, AR-C239
RL: BIOL (Biological study)
(blood pressure response to, after injection into nucleus reticularis lateralis, alpha-adrenergic receptor subtypes in)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:96671 CAPLUS
DOCUMENT NUMBER: 106:96671
TITLE: Alpha-1 adrenergic receptor binding and contraction of rat caudal artery
AUTHOR(S): Abel, Peter W.; Minneman, Kenneth P.
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: J. Pharmacol. Exp. Ther. (1986), 239(3), 678-86
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

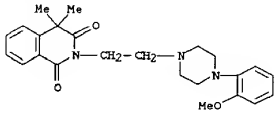
AB Alpha-1 adrenergic receptors were examd. in rat caudal artery by using radioligand binding of 125I-labeled BE 2254 [40077-13-2] (125IBE) and in vitro contraction measurements. 125IBE bound rapidly and reversibly to a single class of high-affinity binding sites in membrane prepns. of caudal artery. Scatchard anal. gave an equil. dissocn. const. (KD) of 110 pM and a d. of binding sites of 115 fmol/mg of protein. Antagonists inhibited 125IBE binding and phenylephrine [59-42-7]-induced contractions competitively, with an order of potency of prazosin [19216-56-9] > ARC 239 [**67339-62-2**] > phentolamine [50-60-2] > yohimbine [146-48-5]. The pA2 (neg. log of antagonist concn. producing a half-max. effect) values for inhibition of phenylephrine-induced contraction correlated well with KD values for inhibition of specific 125IBE binding. A no. of other full and partial agonists also caused contraction of caudal arteries with an order of potency of epinephrine [51-43-4] > norepinephrine [51-41-2] > phenylephrine > methoxamine [390-28-3]. The order of potency of agonists and the potencies of antagonists suggests that the contractile responses of rat caudal artery were mediated by alpha-1 adrenergic receptors. The 50% effective concn. (EC50) values of partial agonists in causing contraction correlated well with their KD values for inhibition of specific 125IBE binding. However, the EC50 values for full agonists were 30-200-fold lower than their KD values. Treatment of caudal arteries in vitro with 0.1 .mu.M phenoxybenzamine for 10 min to inactivate alpha adrenergic receptors decreased both the potency of full agonists in causing contraction and the maximal contractile response. Functional equil. dissocn. consts. calcd. from contraction expts. using pheoxybenzamine agreed well with KD's detd. from binding studies; however, phenoxybenzamine reduced 125IBE binding sites by 50%, whereas the theor. redn. in functional alpha adrenergic receptors averaged

L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

96%. Apparently, 125IBE labels the alpha-1 adrenergic receptors mediating contraction of rat caudal artery. When receptor d. is reduced, the potencies of agonists in activating the receptors agree well with their potencies in binding to the receptors, suggesting that there is a pool of spare alpha-1 adrenergic receptors in this tissue.

IT **67339-62-2**, ARC 239
RL: BIOL (Biological study)
(caudal artery contraction by phenylephrine and .alpha.1-adrenergic ligand binding antagonism by)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

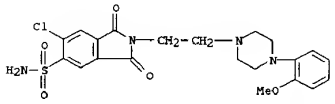


L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:424279 CAPLUS
DOCUMENT NUMBER: 105:24279
TITLE: 2-(1-Piperazinylalky)-1-oxo-1H-isoindoles
INVENTOR(S): Dolak, Terence M.
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Ger. Offen., 84 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

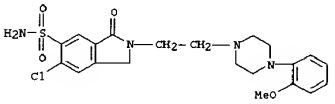
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3524635	A1	19860123	DE 1985-3524635	19850710
US 4585773	A	19860429	US 1984-629649	19840711
CA 1255311	A1	19890606	CA 1985-485831	19850628
ZA 8505092	A	19860226	ZA 1985-5092	19850705
FI 8502694	A	19860112	FI 1985-2694	19850708
FI 79837	B	19891130		
FI 79837	C	19900312		
SE 8503415	A	19860112	SE 1985-3415	19850709
SE 457449	B	19881227		
SE 457449	C	19890420		
ES 545003	A1	19870501	ES 1985-545003	19850709
BE 902847	A1	19860110	BE 1985-215319	19850710
DK 8503150	A	19860112	DK 1985-3150	19850710
DK 163057	B	19920113		
DK 163057	C	19920609		
NO 8502779	A	19860113	NO 1985-2779	19850710
NO 163775	B	19900409		
AU 8544764	A1	19860116	AU 1985-44764	19850710
AU 584104	B2	19890518		
FR 2567519	A1	19860117	FR 1985-10587	19850710
FR 2567519	B1	19900413		
GB 2161807	A1	19860122	GB 1985-17418	19850710
GB 2161807	B2	19871209		
HU 39177	A2	19860828	HU 1985-2669	19850710
HU 195213	B	19880428		
NL 8501998	A	19860203	NL 1985-1998	19850711
JP 61036260	A2	19860220	JP 1985-153333	19850711
JP 04000066	B4	19920106		
AT 8502062	A	19870815	AT 1985-2062	19850711
AT 385270	B	19880310		
CH 664964	A	19880415	CH 1985-3016	19850711
JP 61178964	A2	19860811	JP 1985-271277	19851202
ES 552108	A1	19870801	ES 1986-552108	19860217
NO 8703462	A	19860113	NO 1987-3462	19870817
DK 9100066	A	19910114	DK 1991-66	19910114

PRIORITY APPLN. INFO.: US 1984-629649 19840711
NO 1985-2779 19850710
OTHER SOURCE(S): CASREACT 105:24279
GI

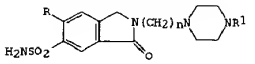
L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



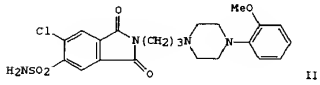
IT **102391-72-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antihypertensive and diuretic)
RN 102391-72-0 CAPLUS
CN 1H-Isoindole-5-sulfonamide,
6-chloro-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-
1-piperazinyl]ethyl]-3-oxo- (9CI) (CA INDEX NAME)



L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



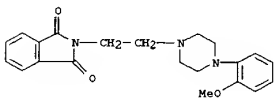
I



II

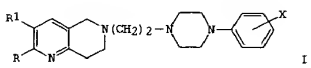
AB The title compds. [I; R = halo, F3C; R1 = (un)substituted Ph, PhCH2, Bz,
2-pyridyl; n = 2-5] were prepd. as antihypertensives and diuretics. Thus,
1-(2-methoxyphenyl)piperazine was quant. condensed with
N-(3-bromopropyl)phthalimide and the product deprotected with N2H4 to give
95% 1-(3-aminopropyl)-4-(2-methoxyphenyl)piperazine. This was condensed
with 4-chloro-5-sulfamoylphthalimide to give 61%
(piperazinylpropyl)phthalimide II which was selectively reduced with Zn in
HOAc to give 77% I (R = Cl, R1 = 2-MeOC6H4) (III). In rats 30 mg III/kg
reduced blood pressure 84 mmHg.

IT **99718-67-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrazinolysis of)
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



IT **102391-88-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 102391-88-8 CAPLUS
CN 1H-Isoindole-5-sulfonamide,
6-chloro-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-
1-piperazinyl]ethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:141729 CAPLUS
DOCUMENT NUMBER: 104:141729
TITLE: Antivertigo agents. V. Quantitative structure-activity relationships of
6-[2-(4-aryl-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-1,6-naphthyridines
AUTHOR(S): Shiozawa, Akira; Kogo, Yoshiya; Ichikawa, Yuhichiro;
Komuro, Chikara; Ishikawa, Michio; Kurashige, Shuji;
Miyazaki, Hiroshi; Yamanaka, Hiroshi; Sakamoto, Takao
CORPORATE SOURCE: Res. Lab., Nippon Kayaku Co., Tokyo, 115, Japan
SOURCE: Chem. Pharm. Bull. (1985), 33(12), 5332-40
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



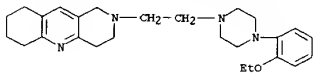
I

AB The quant. structure-activity relationships (QSAR) between the mol. structures and antivertigo activities of
6-[2-(4-aryl-1-piperazinyl)ethyl]-
5,6,7,8-tetrahydro-1,6-naphthyridines I (R1R2 = (CH2)4; R1 = R2 = H; X= H,
F, Cl, Me, NMe2, OMe, OEt, SMe, etc.) were investigated. The effects of
the ortho-, meta-, and para-substituents on the Ph ring of the arylpiperazine moiety were examd. by means of regression anal. using various physicochem. parameters related to these substituents. The results showed that only the parameters concerning the ortho-substituent
were statistically significant. Namely, the relative activity depended on
both Fortho (Swain-Lupton field effect const. of the ortho-substituent)
and I (indicator variable for the presence of an o-alkoxy group and an o-dimethylamino group). Thus, regression anal. for only the ortho-substituted compds. was examd. and afforded a result similar to that
described above. Further, the net at. charge calcd. by the MO method besides free energy-related substituent parameters was used as electronic
parameters of the ortho-substituents on the Ph ring for this QSAR anal.
For the ortho-substituted compds. alone, the potency correlated well with

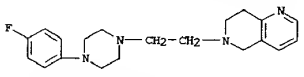
the net at. charge on the first atom of the ortho-substituent (Qortho),
while the correlation for all the compds. (ortho-, meta-, and para-substituents) was slightly lower than that for the ortho-substituted
compds. alone. It was found that increase in the neg. net at. charge on
the first atom of the ortho-position increased the relative activity. The
correlation between Qortho, and Fortho and I was examd. and the role of I
is discussed in connection with H bond-forming ability. The interaction
between the arylpiperazine moiety in the compd. and a putative receptor is
discussed based on the QSAR anal.

IT **83081-77-0 83082-17-1 83082-23-9 83082-27-3 83082-29-5 83082-65-9 83100-19-0 83100-22-5 83100-24-7 83100-35-0 95355-89-8 95355-91-2 95355-93-4 95355-95-6 95355-97-8 95355-99-0 95356-01-7 95356-06-2 95356-07-3 95356-08-4 95356-09-5 95356-10-8 95356-11-9 95356-12-0 95356-13-1 95356-14-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antivertigo activity of, structure in relation to)

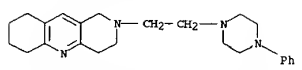
RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



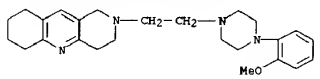
RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



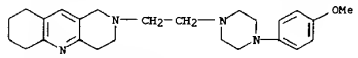
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-



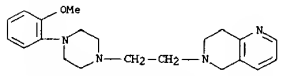
RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



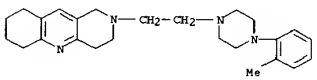
RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



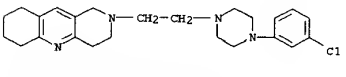
RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



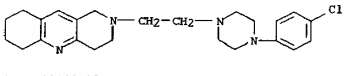
RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



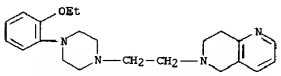
RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



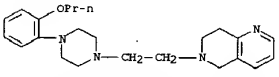
RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



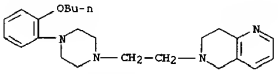
RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



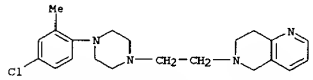
RN 95355-89-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-propoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



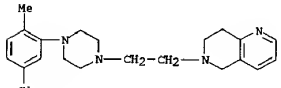
RN 95355-91-2 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



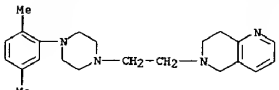
RN 95355-93-4 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



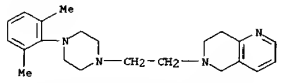
RN 95355-95-6 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



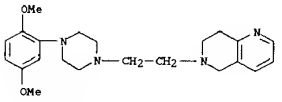
RN 95355-97-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



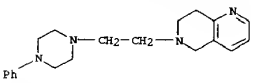
RN 95355-99-0 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



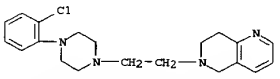
RN 95356-01-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-
5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



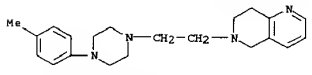
RN 95356-06-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-
(9CI) (CA INDEX NAME)



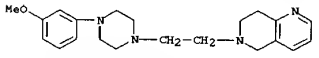
RN 95356-07-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



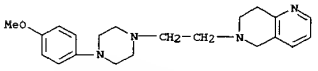
RN 95356-08-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



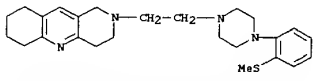
RN 95356-13-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



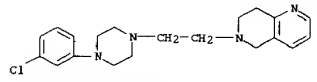
RN 95356-14-2 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



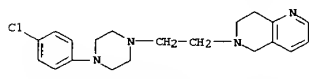
IT **89009-91-6P 101413-03-0P 101413-04-1P**
101413-05-2P 101413-06-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antivertigo activity of, structure in relation to)
RN 89009-91-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



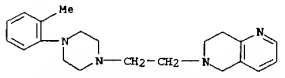
RN 101413-03-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



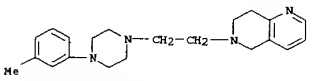
RN 95356-09-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



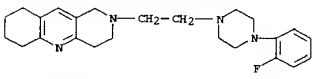
RN 95356-10-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



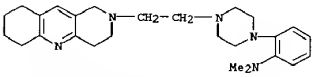
RN 95356-11-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



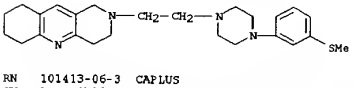
RN 95356-12-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



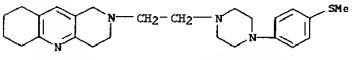
RN 101413-04-1 CAPLUS
CN Benzenamine,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-
yl)ethyl]-1-piperazinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101413-05-2 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[3-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



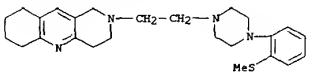
RN 101413-06-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[4-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT **89009-95-0P 101413-07-4P 101413-08-5P**
101413-09-6P 101413-10-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 89009-95-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-
(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)
(9CI)
(CA INDEX NAME)

CM 1

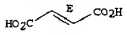
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 89009-91-6
CMF C25 H34 N4 S



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

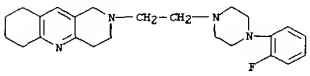
Double bond geometry as shown.



RN 101413-07-4 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX
NAME)

CM 1

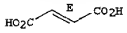
CRN 101413-03-0
CMF C24 H31 F N4



CM 2

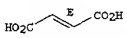
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

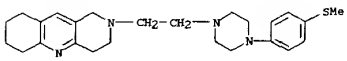
Double bond geometry as shown.



RN 101413-10-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[4-
(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)
(9CI)
(CA INDEX NAME)

CM 1

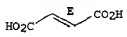
CRN 101413-06-3
CMF C25 H34 N4 S



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

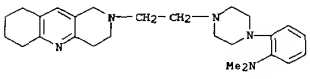


L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 101413-08-5 CAPLUS
CN Benzenamine,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-
yl)ethyl]-1-piperazinyl]-N,N-dimethyl-, (2E)-2-butenedioate (1:2)
(9CI)
(CA INDEX NAME)

CM 1

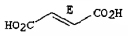
CRN 101413-04-1
CMF C26 H37 N5



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

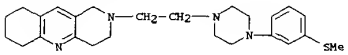
Double bond geometry as shown.



RN 101413-09-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[3-
(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)
(9CI)
(CA INDEX NAME)

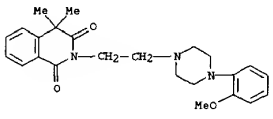
CM 1

CRN 101413-05-2
CMF C25 H34 N4 S



CM 2

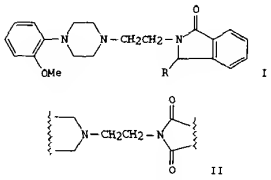
L14 ANSWER 214 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:61789 CAPLUS
DOCUMENT NUMBER: 104:61789
TITLE: Further investigations on the
.alpha.1-adrenoceptor
blocking properties of AR-C 239 in rats
AUTHOR(S): Huchet, Anne Marie; Andrejak, Michel; Lucet,
Bernadette; Gautret, Bruno; Doursout, Marie
Francoise;
Ostermann, Gerard; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med. Broussais, Paris,
75006,
Fr.
SOURCE: Clin. Exp. Pharmacol. Physiol. (1985), 12(5),
505-13
CODEN: CEXPB9; ISSN: 0305-1870
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AR-C 239 [**67339-62-2**], an .alpha.-adrenoceptor-blocking drug,
appears to act selectively on .alpha.1 sites in rats. At peripheral
sites, this drug did not change the tachycardia induced by spinal
sympathetic outflow stimulation in pithed rats, and did not
antagonize the
inhibitory effects of clonidine on this prepn. In addn., AR-C 239
showed
predominant .alpha.1-adrenoceptor-blocking properties in the bisected
rat
vas deferens prepn. AR-C 239 did not prevent or reverse the centrally
mediated hypotensive and bradycardic actions induced by clonidine, in
intact animals. Thus, AR-C 239 seems to be a very useful tool for the
characterization of peripheral and central .alpha.1-adrenoceptors, in
this
animal species.
IT **67339-62-2**
RL: BIOL (Biological study)
(as .alpha.1-sympatholytic)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:34108 CAPLUS
DOCUMENT NUMBER: 104:34108
TITLE: 2-Methoxyphenylpiperazine derivatives.
INVENTOR(S): Nagano, Hiroyuki; Takagi, Michiro; Kubodera, Noboru; Matsunaga, Isao; Nahata, Hiroyuki; Oba, Yasuhiro; Sakai, Kazunari; Uchida, Yasuyoshi
PATENT ASSIGNEE(S): Chugai Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 2 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60169461	A2	19850902	JP 1984-24074	19840210
JP 03053301	B4	19910814		

OTHER SOURCE(S): CASREACT 104:34108
GI



I

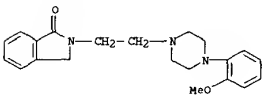
II

AB Title compds. I (R = H, OH) and their salts, useful as cardiovascular agents (no data), were prepd. Thus, stirring 2.88 g 1I and 800 mg NaBH4 in MeOH at room temp. for 5 h gave 2.3 g I (R = OH).

IT **99718-68-0P 99718-69-1P 99718-70-4P 99718-71-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agent)

RN 99718-68-0 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

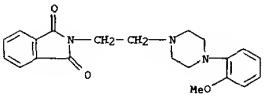
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



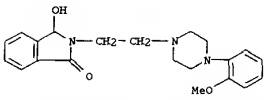
●x HCl

IT **99718-67-9**
RL: RCT (Reactant)
(redn. of, with sodium borohydride)

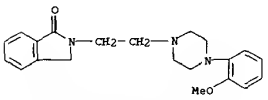
RN 99718-67-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



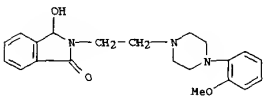
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 99718-69-1 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 99718-70-4 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

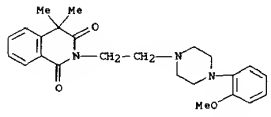
RN 99718-71-5 CAPLUS
CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:499213 CAPLUS
DOCUMENT NUMBER: 103:99213
TITLE: [3H]-Rauwolscine binding to .alpha.2-adrenoceptors in the mammalian kidney: apparent receptor heterogeneity between species
AUTHOR(S): Neylon, C. B.; Summers, R. J.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Melbourne, Parkville, 3052, Australia
SOURCE: Br. J. Pharmacol. (1985), 85(2), 349-59
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

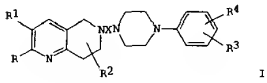
AB Binding of the .alpha.2-adrenoceptor antagonist 3H-labeled rauwolscine [131-03-3] was characterized in membrane prepns. from the kidneys of mouse, rat, rabbit, dog, and man. In all species, binding reached equil. within 45 min and dissocd. at a single exponential rate after addn. of phentolamine 10 .mu.M. Satn. studies showed that the affinity of [3H]rauwolscine was similar in all species (2.33-3.03 nM) except man where it was higher (0.98 nM). Marked differences were seen in the d. of binding sites, increasing in the order: man < dog < rabbit < rat < mouse. In all cases, Hill coeffs. were not different from unity. [3H]rauwolscine binds with low affinity (dissocn. const. KD > 15 nM) to membranes prepd. from guinea-pig kidney. The low affinity binding is not due to the absence of particular ions in the incubation medium or to receptor occupation by endogenous agonist. The binding in all species was stereoselective with respect to the isomers of noradrenaline. However, differences were seen in the characteristics of agonist interactions with the binding site both between isomers and between species. Marked differences in affinity of particular .alpha.-adrenoceptor antagonists were obsd. for .alpha.2-adrenoceptors labeled by [3H]rauwolscine. These differences were most evident with the .alpha.1-adrenoceptor selective antagonist prazosin [19216-56-9] which displayed inhibition consts. (Ki values) of 33.2, 39.5, 261, 570, and 595 nM in rat, mouse, dog, man, and rabbit, resp. Differences are apparent in the characteristics of .alpha.2-adrenoceptors labeled by [3H]rauwolscine between species and the differences obsd. for .alpha.1-selective antagonists such as prazosin may be related to binding to addnl. sites in the vicinity of the .alpha.2-adrenoceptor.

IT **67339-62-2**
RL: BIOL (Biological study)
(.alpha.2-adrenoceptor binding of, in kidney of human and lab. animals,

L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
species variations in)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



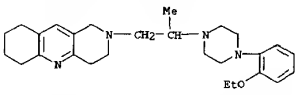
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:149226 CAPLUS
DOCUMENT NUMBER: 102:149226
TITLE: Antivertigo agents. 1V. Synthesis and antivertigo activity of 6-[.omega.-(4-aryl-1-piperazinyl)alkyl]-5,6,7,8-tetrahydro-1,6-naphthyridines
AUTHOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Komuro, Chikara; Ishikawa, Michio; Furuta, Yasuhiko; Kurashige, Shuji; Miyazaki, Hiroshi; Yamanaka, Hiroshi; Sakamoto, Takao
CORPORATE SOURCE: Res. Lab. Pharm. Div., Nippon Kayaku Co., Tokyo, 115, Japan
SOURCE: Chem. Pharm. Bull. (1984), 32(10), 3981-93
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



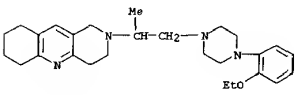
I

AB 6-[.omega.-(4-Aryl-1-piperazinyl)alkyl]-5,6,7,8-tetrahydro-1,6-naphthyridines I [R, R1 = H, Me; RR1 = (CH2)4; R2 = H, 5-Me 7-Me, 8-Me; R3 = H, F, Cl, Me, alkoxy; R4 = H, Cl; Me, OMe; X = alkylene] (50 compds.) were synthesized and evaluated for antivertigo activity be testing their ability to inhibit spontaneous nystagamus in cats. Structure-activity relationships are discussed. Many I having the 4-(2-alkoxyphenyl)piperazine group showed more potent antivertigo activity than diphenidol. Among them, I [RR1 = (CH2)4, R2 = R4 = H, R3 = 2-EtO, X = CH2CH2] was selected as a promising antivertigo agent. This compd, also exhibited a more potent inhibitory effect on apomorphine-induced vomiting in dogs than diphenidol.
IT **83081-59-8P 83081-71-4P 83081-72-5P**
83081-73-6P 83081-76-9P 83081-77-0P
83081-78-1P 83082-17-1P 83082-18-2P
83082-23-9P 83082-24-0P 83082-27-3P
83082-28-4P 83082-29-5P 83082-30-8P
83082-37-5P 83082-38-6P 83082-59-1P
83082-61-5P 83082-62-6P 83082-65-9P

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
83082-67-1P 83100-13-4P 83100-14-5P
83100-17-8P 83100-18-9P 83100-19-0P
83100-20-3P 83100-22-5P 83100-23-6P
83100-24-7P 83100-25-8P 83100-35-0P
83100-36-1P 84328-17-6P 95355-89-8P
95355-90-1P 95355-91-2P 95355-92-3P
95355-93-4P 95355-94-5P 95355-95-6P
95355-96-7P 95355-97-8P 95355-98-9P
95355-99-0P 95356-00-6P 95356-01-7P
95356-02-8P 95356-03-9P 95356-04-0P
95356-05-1P 95356-06-2P 95356-07-3P
95356-08-4P 95356-09-5P 95356-10-8P
95356-11-9P 95356-12-0P 95356-13-1P
95356-14-2P 95395-61-2P 95395-62-3P
95395-63-4P 95395-64-5P 95395-65-6P
95395-66-7P 95395-67-8P 95395-68-9P
95410-22-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antivertigo activity of)
RN 83081-59-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



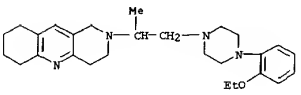
RN 83081-71-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83081-72-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CM 1

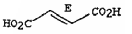
CRN 83081-71-4
CMF C27 H38 N4 O



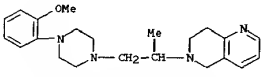
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83081-73-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

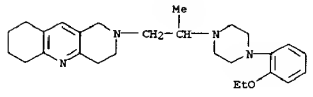


RN 83081-76-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83081-59-8
CMF C27 H38 N4 O

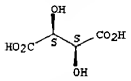
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



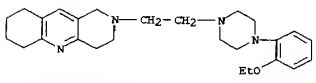
CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

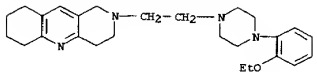


RN 83081-78-1 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

CRN 83081-77-0
CMF C26 H36 N4 O

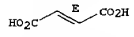
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



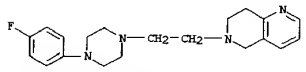
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



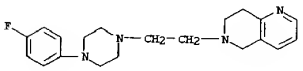
RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



RN 83082-18-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-17-1
CMF C20 H25 F N4

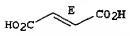


CM 2

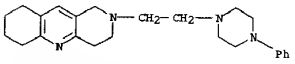
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



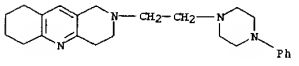
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

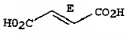
CRN 83082-23-9
CMF C24 H32 N4



CM 2

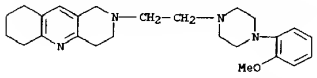
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

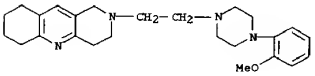
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83082-28-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

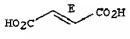
CRN 83082-27-3
CMF C25 H34 N4 O



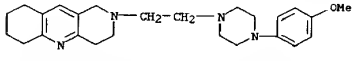
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



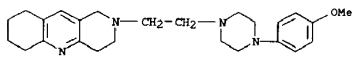
RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA
INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CM 1

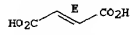
CRN 83082-29-5
CMF C25 H34 N4 O



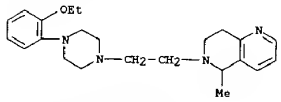
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl- (9CI) (CA INDEX NAME)

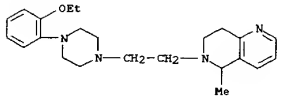


RN 83082-38-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

CRN 83082-37-5
CMF C23 H32 N4 O

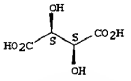
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



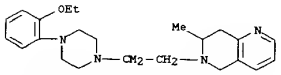
CM 2

CRN 133-37-9
CMF C4 H6 O6

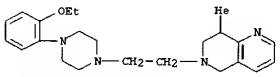
Relative stereochemistry.



RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-methyl- (9CI) (CA INDEX NAME)

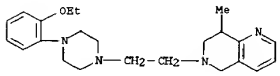


RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

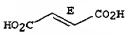
CRN 83082-61-5
CMF C23 H32 N4 O



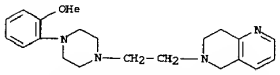
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

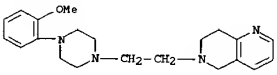


RN 83082-67-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-65-9
CMF C21 H28 N4 O

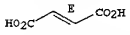
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



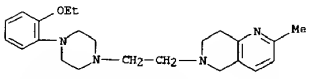
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



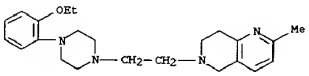
RN 83100-13-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-13-4
CMF C23 H32 N4 O

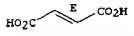


CM 2

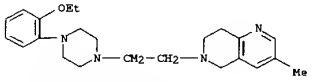
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



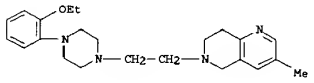
RN 83100-17-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-18-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

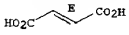
CRN 83100-17-8
CMF C23 H32 N4 O



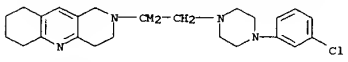
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



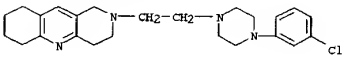
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83100-23-6 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

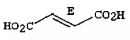
CRN 83100-22-5
CMF C24 H31 Cl N4



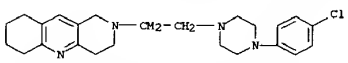
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

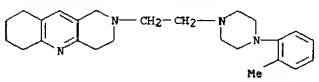


RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX

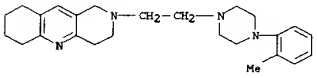
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)

CM 1

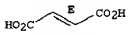
CRN 83100-19-0
CMF C25 H34 N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

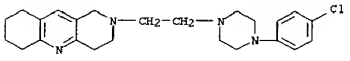


RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
NAME)

CM 1

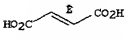
CRN 83100-24-7
CMF C24 H31 Cl N4



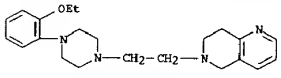
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

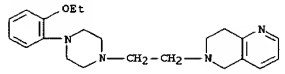


RN 83100-36-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-35-0
CMF C22 H30 N4 O

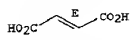
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

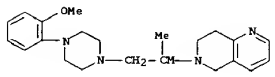
Double bond geometry as shown.



RN 84328-17-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

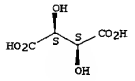
CRN 83081-73-6
CMF C22 H30 N4 O



CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.

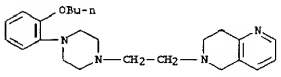


RN 95355-89-8 CAPLUS

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

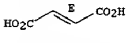
CRN 95355-91-2
CMF C24 H34 N4 O



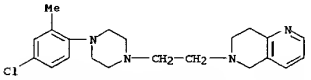
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95355-93-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

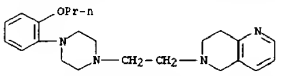


RN 95355-94-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-93-4
CMF C21 H27 Cl N4

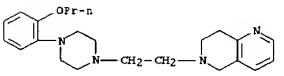
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-propoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95355-90-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-propoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

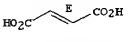
CRN 95355-89-8
CMF C23 H32 N4 O



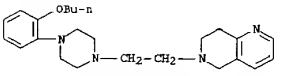
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

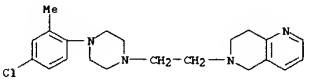


RN 95355-91-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95355-92-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

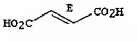
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



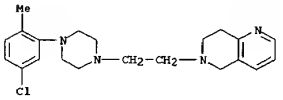
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



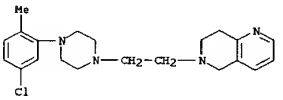
RN 95355-95-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95355-96-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-95-6
CMF C21 H27 Cl N4

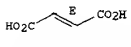


L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

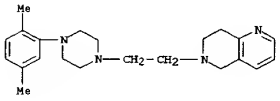
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



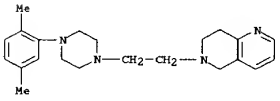
RN 95355-97-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95355-98-9 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-97-8
CMF C22 H30 N4

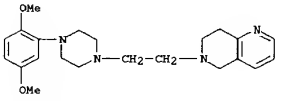


CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

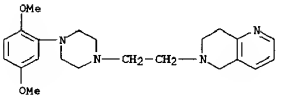
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 95356-02-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

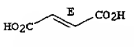
CRN 95356-01-7
CMF C22 H30 N4 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

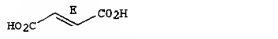


RN 95356-03-9 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

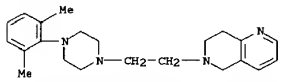
CM 1

CRN 83082-59-1
CMF C23 H32 N4 O

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



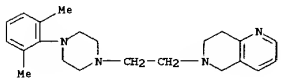
RN 95355-99-0 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95356-00-6 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

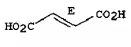
CRN 95355-99-0
CMF C22 H30 N4



CM 2

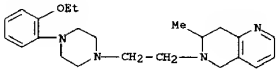
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95356-01-7 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

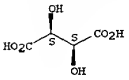
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



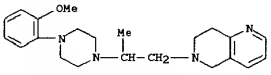
CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



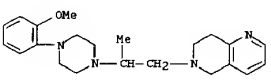
RN 95356-04-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 95356-05-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-04-0
CMF C22 H30 N4 O

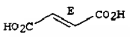


CM 2

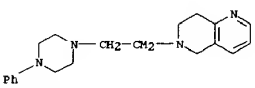
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CMF C4 H4 O4
CDES 2:E

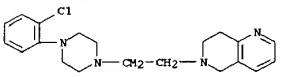
Double bond geometry as shown.



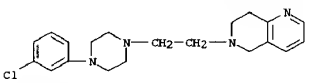
RN 95356-06-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-
(9CI) (CA INDEX NAME)



RN 95356-07-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)

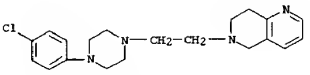


RN 95356-08-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)

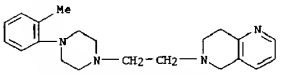


RN 95356-09-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)

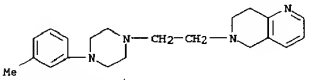
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



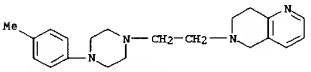
RN 95356-10-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



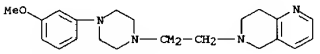
RN 95356-11-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95356-12-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

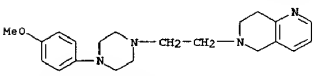


RN 95356-13-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95356-14-2 CAPLUS

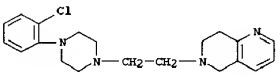
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95395-61-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

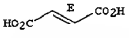
CRN 95356-07-3
CMF C20 H25 Cl N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

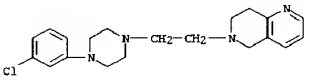


RN 95395-62-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-08-4
CMF C20 H25 Cl N4

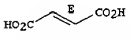
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

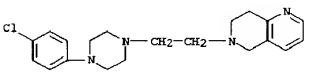
Double bond geometry as shown.



RN 95395-63-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

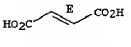
CRN 95356-09-5
CMF C20 H25 Cl N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

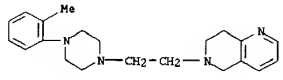
Double bond geometry as shown.



RN 95395-64-5 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

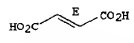
CRN 95356-10-8
CMF C21 H28 N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

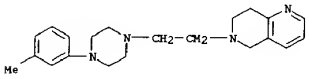
Double bond geometry as shown.



RN 95395-65-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-11-9
CMF C21 H28 N4



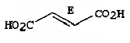
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

CDES 2:E

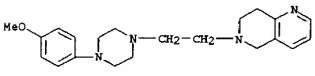
Double bond geometry as shown.



RN 95395-68-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

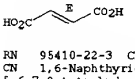
CRN 95356-14-2
CMF C21 H28 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

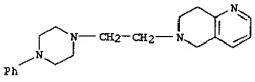
Double bond geometry as shown.

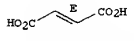


RN 95410-22-3 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-06-2
CMF C20 H26 N4

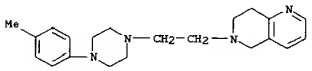




RN 95395-66-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

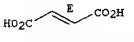
CRN 95356-12-0
CMF C21 H28 N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

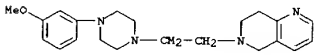
Double bond geometry as shown.



RN 95395-67-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-13-1
CMF C21 H28 N4 O



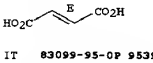
CM 2

CRN 110-17-8
CMF C4 H4 O4

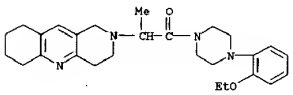
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

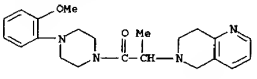
Double bond geometry as shown.



IT **83099-95-0P 95395-47-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 83099-95-0 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

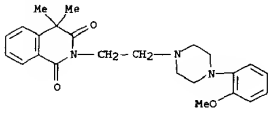


RN 95395-47-4 CAPLUS
CN Piperazine, 1-[2-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1-oxopropyl]-4-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

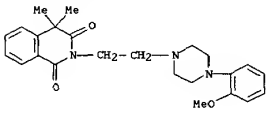


L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:73242 CAPLUS
DOCUMENT NUMBER: 102:73242
TITLE: Calcium influx-dependent and -independent .alpha.1-adrenoceptor-mediated processes of vasoconstriction in vivo do not operate via different .alpha.1-adrenoceptor subtypes
AUTHOR(S): Korstanje, Cornelis; Wilffert, Bob; De Jonge, Adriaan; Thoolen, Martin J. M. C.; Timmermans, Pieter B. M. W.; Van Zwieten, Pieter A.
CORPORATE SOURCE: Dep. Pharm., Univ. Amsterdam, Amsterdam, 1018 TV, Neth.
SOURCE: J. Cardiovasc. Pharmacol. (1984), 6(6), 1102-8
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In pithed rats, the selective .alpha.1-adrenoceptor agonists St 587 [15327-38-5] and cirazoline [59939-16-1] show preponderant Ca influx-dependent and -independent vasoconstriction, resp. Using these agonists, selective (competitive) antagonists for either process of vasoconstriction were sought. For this purpose, antagonism was analyzed for 8 structurally different antagonists (prazosin [19216-56-9], BE 2254 [40077-13-2], AR-C239 [**67339-62-2**], R 28935 [55806-43-4], corynanthine [483-10-3], phentolamine [50-60-2], sulpiride [15676-16-1], and chlorpromazine [50-53-3]) opposing the pressor responses evoked by cirazoline and St 587. Where pA2 values (-log dose antagonist evoking a 2-fold shift for the agonist dose-response curve) could be calcd., no significantly different pA2 values against either agonist resulted. However, with respect to the slopes of the Schild plots, deviations from 1 were found for prazosin, R 28935, AR-C239, sulpiride, and chlorpromazine, but not uniformly against both agonists. Following treatment with phenoxybenzamine (PB) (30 .mu.g/kg) and nifedipine (1 mg/kg), which produced Ca influx-sensitive and -insensitive vasoconstriction to cirazoline, resp., Schild plots were constructed for BE 2254, prazosin, and chlorpromazine. Using cirazoline as an agonist, unity slopes were now obtained for prazosin and chlorpromazine. The Schild plots of BE 2254 vs. cirazoline after PB or nifedipine administration, however, exhibited a slope deviating from 1. For prazosin and chlorpromazine, identical pA2 values still resulted against both processes of vasoconstriction to cirazoline. Evidently, .alpha.1-adrenoceptors mediating Ca influx-dependent and -independent vasoconstriction in vivo are not distinctly different entities, but are sep. recognition sites of the same receptor.

L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT **67339-62-2**
RL: BIOL (Biological study)
(blood vessel contraction inhibition by, adrenergic receptors and calcium in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



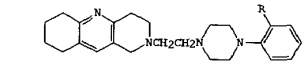
L14 ANSWER 219 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:604190 CAPLUS
DOCUMENT NUMBER: 101:204190
TITLE: Non-specific, time-dependent desensitization of the vas deferens and anococcygeus preparations of the rat to .alpha.1-adrenoceptor antagonists and atropine
AUTHOR(S): Onnen, Igor
CORPORATE SOURCE: Fac. Med., Univ. Paris-Nord, Bobigny, Fr.
SOURCE: Br. J. Pharmacol. (1984), 83(1), 7-14
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat vas deferens prepns. became desensitized to the .alpha.1-adrenoceptor antagonist thymoxamine [54-32-0]: after 6 h in vitro, the 4 value (time to attain half the occupancy of receptors occupied at equil.) of the response to this drug was 1.50 fold greater in control strips (strips exposed to thymoxamine at 6 h) than in test strips (strips exposed to thymoxamine at 1 h). The rate of action of the .alpha.1-adrenoceptor antagonist AR-C239 [**67339-62-2**] on the rat anococcygeus prepn. was correlated with the rate of action of atropine [51-55-8]. There was also a significant correlation between the 4 ratios (1.37 and 1.30 for AR-C239 an atropine resp.) obsd. in the control muscles at 6 h. The in vitro slowing is thus due to some change in the longitudinal muscle and not to a change in the receptors. The in vitro slowing occurred when either phenylephrine or methoxamine was the .alpha.1-adrenoceptor agonist used. The most likely mechanism of desensitization is a non-specific slowing of the access of drugs to receptors.
IT **67339-62-2**
RL: BIOL (Biological study)
(vas deferens and anococcygeus muscle desensitization to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



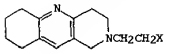
L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:103395 CAPLUS
DOCUMENT NUMBER: 100:103395
TITLE: 1,2,3,4,6,7,8,9-Octahydro-benzo[b]-1,6-naphthyridine derivatives
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58188884	A2	19831104	JP 1982-70338	19820428

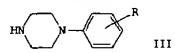
GI



I



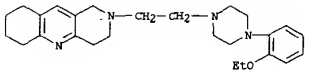
II



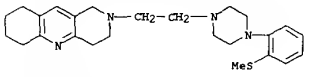
III

AB Title compds. I (R = MeS, EtO, BzO) were prepd. by reaction of II (X = halo) with III (R = MeS, EtO) optionally followed by hydrolysis and benzoylation. Antivertigo and muscle relaxation activity test data of I were shown in cats and mice, resp. Thus, refluxing a mixt. of II 2HCl (X = Cl) 4.9, III HCl (R = O-MeS) 3.7, and Et3N 7.6 g in EtOH 2 h gave 76% I (R = MeS), which was converted to the fumarate by treating with fumaric acid in Me2CO.
IT **83081-77-0P 89009-91-6P 89009-92-7P**
89009-94-9P 89009-95-0P 89009-96-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and pharmacol. activities of)
RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

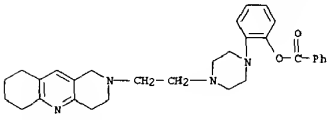
L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 89009-91-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 89009-92-7 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester) (9CI) (CA INDEX NAME)

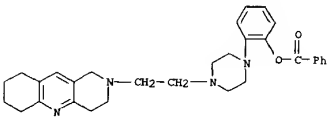


RN 89009-94-9 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester), (2E)-2-butenedioate (1:2)
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 89009-92-7
CMF C31 H36 N4 O2

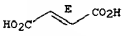
L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

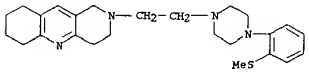
Double bond geometry as shown.



RN 89009-95-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

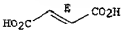
CRN 89009-91-6
CMF C25 H34 N4 S



CM 2

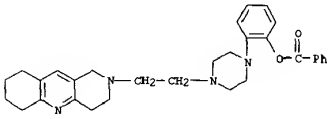
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 89009-96-1 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester), tetrahydrochloride (9CI) (CA
INDEX NAME)



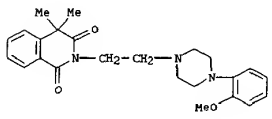
●4 HCl

L14 ANSWER 221 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:497179 CAPLUS
DOCUMENT NUMBER: 99:97179
TITLE: Structure of 2-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-1,3(2H,4H)-isoquinolinedione hydrochloride-ethanol (AR-C239), C24H30N3O3+.Cl-.C2H6O
AUTHOR(S): Carpy, Alain; Goursolle, Michel; Leger, Jean Michel
CORPORATE SOURCE: Fac. Pharm., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: Acta Crystallogr., Sect. C: Cryst. Struct. Commun.
(1983), C39(8), 1087-9
CODEN: ACSCEE
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The title compd. is triclinic, space group P.hivin.1, was a 9.749(2), b
11.287(5), c 13.815(1) .ANG., .alpha. 77.43(2), .beta. 83.99(1), and .gamma. 69.96(3).degree.; Z = 2 for dc = 1.17. Final R = 0.070 for 2643
reflections. The bridge chain is in the fully extended conformation and
is perpendicular to the isoquinoline plane. N-H...Cl H-bonds contribute
to the cryst. cohesion. At. coordinates are given.
IT **86891-01-2**
RL: PRP (Properties)
(structure of)
RN 86891-01-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride, compd. with ethanol
(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 86891-00-1
CMF C24 H29 N3 O3 . Cl H

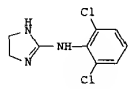


● HCl

L14 ANSWER 221 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CM 2

CRN 64-17-5
CMF C2 H6 O

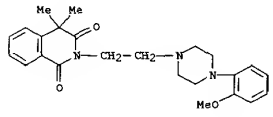
L14 ANSWER 222 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:432919 CAPLUS
DOCUMENT NUMBER: 99:32919
TITLE: Bronchopulmonary effects of clonidine on the bronchomotor responses of the guinea pig
AUTHOR(S): Advenier, Charles; Floch, Anne; Mallard, Brigitte
CORPORATE SOURCE: Lab. Pharmacol., Fac. Med. Paris, Paris, F-75270, Fr.
SOURCE: Eur. J. Pharmacol. (1983), 89(1-2), 85-94
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



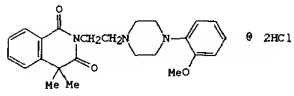
I

AB In conscious guinea pigs, clonidine (I) [4205-90-7] (10 and 100 .mu.g/kg, i.v.) lowered diastolic (-7.9 and -12.4%) and systolic (-8.6 and -11.9%) arterial pressure and reduced heart rate (-14.5 and -27.7%), but did not significantly modify pulmonary airway resistance. Hypotension was suppressed by yohimbine [146-48-5] and bradycardia was partially suppressed by atropine [51-55-8] and yohimbine, which demonstrates in this animal an .alpha.2-adrenergic effect for hypotension and a mixed cholinergic and .alpha.2-adrenergic effect for bradycardia. Clonidine (10 and 100 .mu.g/kg, i.v.) enhanced the bronchoconstrictor effects of histamine [51-45-6] 20 .mu.g/kg (+80.0 and 89.1%), acetylcholine [51-84-3] 25 .mu.g/kg (+66.4 and +55.4%) and serotonin creatinine sulfate [971-74-4] 15 .mu.g/kg (+68.5 and +81.4%). The duration of this effect was comparable to that of the hypotensive and cardiac effects of clonidine. The effects of clonidines were suppressed after pretreatment with propranolol [525-66-6], reserpine [50-55-5], or pentobarbitone [76-74-4], all drugs which enhance the bronchoconstrictor effect of acetylcholine. Yohimbine (1 mg/kg), piperoxan [59-39-2] (0.3 mg/kg) or prazosin [19216-56-9] in high dosage (0.3 mg/kg) inhibited the potentiation by clonidine of acetylcholine-induced bronchoconstriction, whereas prazosin in lower doses (0.03 mg/kg) or AR-C 239 [**67339-62-2**] (0.05 mg/kg) had no action. A specific involvement of .alpha.2-adrenoceptors stimulated by clonidine with subsequent redn. of the adrenergic activity assocd. with bronchospasm could therefore be

L14 ANSWER 222 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
demonstrated in the conscious guinea-pig during bronchomotor reactions.
IT **67339-62-2**
RL: BIOL (Biological study)
(bronchopulmonary effects of clonidine in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



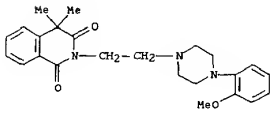
L14 ANSWER 223 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:172852 CAPLUS
DOCUMENT NUMBER: 98:172852
TITLE: AR-C239 a new and potent .alpha.-adrenoceptor blocking drug
AUTHOR(S): Mouille, P.; Huchet, A. M.; Chelly, J.; Schmitt, H.
CORPORATE SOURCE: Lab. Pharmacol., Fac. Broussais, Paris, Fr.
SOURCE: Alpha-Bloquants, Symp. Int. (1981), Meeting Date 1979, 14-20. Masson: Paris, Fr.
CODEN: 49LNA7
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I

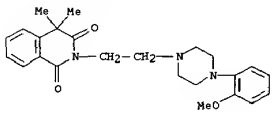
AB The pharmacol. effects of AR-C 239 (I) [**67339-62-2**] (30-50 mg/kg, i.v.) were investigated in anesthetized dogs. I produced a long-lasting fall in blood pressure and cardiac parameters partly by acting peripherally and partly by central redn. in sympathetic nerve activity. I was specific for .alpha.1-postsynaptic adrenoceptors in dogs. The cardiovascular effects of clonidine and the baroreceptor reflex were unaffected by I, indicating that adrenoceptors implicated in these effects are of the .alpha.2-type. I may be useful in the characterization of .alpha.-adrenoceptors.
IT **67339-62-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 223 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 224 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:84010 CAPLUS
DOCUMENT NUMBER: 98:84010
TITLE: The .alpha.2-adrenergic receptor of human fat cells.
comparative study of .alpha.2-adrenergic radioligand
binding and biological response
AUTHOR(S): Berlan, Michel; Lafontan, Max
CORPORATE SOURCE: Fac. Med., Univ. Paul Sabatier, Toulouse, F-31400, Fr.
SOURCE: J. Physiol. (Paris) (1982), 78(3), 279-87
CODEN: JOPHAN; ISSN: 0021-7948
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding of 3H-labeled yohimbine (I) [146-48-5], an .alpha.2-adrenergic antagonist, and clonidine (II) [4205-90-7], an .alpha.2-adrenergic agonist, on the human fat cell membrane .alpha.-adrenoceptor was compared. The relative order of affinity of various agonists and antagonists towards the .alpha.-receptor with their relative biol. potency when estd. by measuring the lipolysis rate of adipocytes in vitro were also compared. The specific binding of these 2 radioactive ligands was a saturable process. The estd. equil. dissocn. consts. (KD) were similar (4 nM for [3H]II, and 4.3 nM for [3H]I). The no. of [3H]I-binding sites per mg protein was .apprx.2-3 times higher than the no. of [3H]II-binding sites (350 fmol/mg protein). The relative order of potency of various .alpha.-agonists and .alpha.-antagonists in competition with the 2 radioligands was similar and was consistent with the delineation of an .alpha.2-adrenoceptor. For integrated anal. at the cellular level, the effect of the various .alpha.-adrenomimetics on theophylline and isoproterenol-induced lipolysis was also studied. Substances which possess .alpha.2-adrenomimetic potency induce an antilipolytic effect whereas .alpha.1-adrenomimetic drugs were without effect. Moreover the order of potency of .alpha.-antagonists in the suppression of the antilipolysis promoted by II is in good agreement with the involvement of an .alpha.2-adrenoceptor stimulation in the genesis of the inhibiting effect on lipolysis. The binding sites of I and II on human fat cell membranes apparently correspond to the physiol. .alpha.2-adrenergic receptors involved in the antilipolytic effect of catecholamines in human adipose tissue.
IT **67339-62-2**
RL: PROC (Process)
(adrenergic receptor binding of, in adipocyte of human, lipolysis in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-

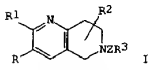
L14 ANSWER 224 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:72076 CAPLUS
DOCUMENT NUMBER: 98:72076
TITLE: 5,6,7,8-Tetrahydro-1,6-naphthyridine derivatives
INVENTOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Ishikawa, Michio; Miyazaki, Hiroshi; Yamanaka, Hiroshi
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Fr. Demande, 108 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2492825	A1	19820430	FR 1981-20262	19811028
JP 57075983	A2	19820512	JP 1980-150719	19801029
ES 507200	A1	19830201	ES 1981-507200	19811029

PRIORITY APPLN. INFO.: JP 1980-150719 19801029
GI

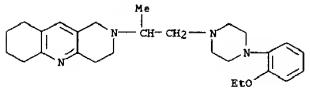


I

AB Naphthyridines I (R and R1 are H, alkyl, or RR1 = C2-5 alkylene; R2 = H, alkyl, PhCH2, Ph, halo-, alkyl-, or alkoxyphenyl; Z = C2-4 alkylene; R3 = dialkylamine, 1-pyrrolidinyl, 1-piperidinyl, a 4-hydroxy-4-phenyl-1-piperidinyl group, 4-morpholinyl, a 4-substituted 1-piperazinyl group) were prepd., and they showed anti-vertigo and muscle relaxant activity. 5,6,7,8-Tetrahydro-3-methyl-1,6-naphthyridine was treated with 1-(2-chloroethyl)-4-(2-chlorophenyl)piperazine·2HCl and Me3N to give I [R = Me, Z = CH2CH2, R3 = 4-(2-chlorophenyl)-1-piperazinyl, R1 = R2 = H].
IT **83081-72-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and anti-vertigo activity of)
RN 83081-72-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

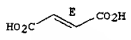
CRN 83081-71-4
CMF C27 H38 N4 O



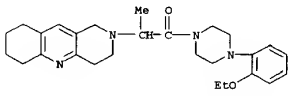
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



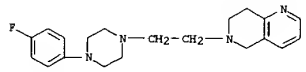
IT **83099-95-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)
RN 83099-95-0 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)



IT **83082-18-2P 83082-28-4P 84328-17-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and muscle relaxant activity of)
RN 83082-18-2 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

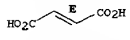
CRN 83082-17-1
CMF C20 H25 F N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

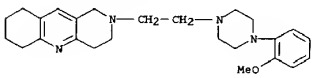
Double bond geometry as shown.



RN 83082-28-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

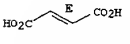
CRN 83082-27-3
CMF C25 H34 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

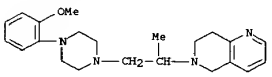


RN 84328-17-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (R*,R*)-2,3-dihydroxybutanedioate (1:2)

(9CI) (CA INDEX NAME)

CM 1

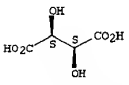
CRN 83081-73-6
CMF C22 H30 N4 O



CM 2

CRN 133-37-9
CMF C4 H6 O6

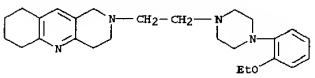
Relative stereochemistry.



IT **83081-78-1P 83082-67-1P 83100-04-3P**
83100-14-5P 83100-18-9P 83100-36-1P
83100-40-7P 84345-54-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and pharmacol. activity of)
RN 83081-78-1 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

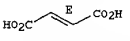
CRN 83081-77-0
CMF C26 H36 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

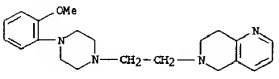
Double bond geometry as shown.



RN 83082-67-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

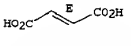
CRN 83082-65-9
CMF C21 H28 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

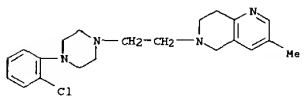


RN 83100-04-3 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

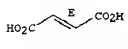
CRN 83100-01-0
CMF C21 H27 Cl N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

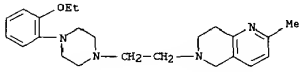
Double bond geometry as shown.



RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-13-4
CMF C23 H32 N4 O



CM 2

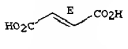
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

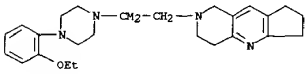
Double bond geometry as shown.



RN 83100-40-7 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

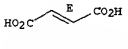
CRN 83100-39-4
CMF C25 H34 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

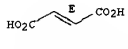


RN 84345-54-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-11-2
CMF C22 H30 N4

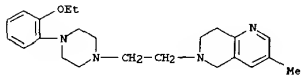
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83100-18-9 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

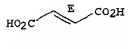
CRN 83100-17-8
CMF C23 H32 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

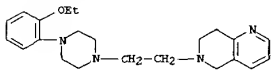
Double bond geometry as shown.



RN 83100-36-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

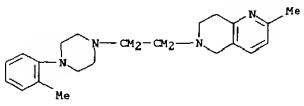
CM 1

CRN 83100-35-0
CMF C22 H30 N4 O



CM 2

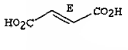
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

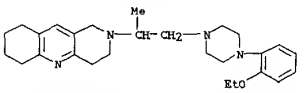
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

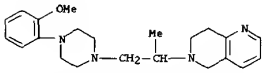


IT **83081-71-4P 83081-73-6P 83081-74-7P**
83081-77-0P 83082-17-1P 83082-23-9P
83082-24-0P 83082-27-3P 83082-29-5P
83082-30-8P 83082-37-5P 83082-59-1P
83082-60-4P 83082-61-5P 83082-62-6P
83082-63-7P 83082-64-8P 83082-65-9P
83100-01-0P 83100-11-2P 83100-13-4P
83100-17-8P 83100-19-0P 83100-20-3P
83100-21-4P 83100-22-5P 83100-23-6P
83100-24-7P 83100-25-8P 83100-26-9P
83100-27-0P 83100-35-0P 83100-37-2P
83100-38-3P 83100-39-4P 84414-63-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 83081-71-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



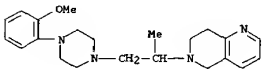
RN 83081-73-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

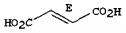
CRN 83081-73-6
CMF C22 H30 N4 O



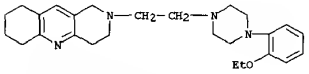
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

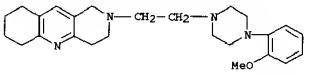
Double bond geometry as shown.



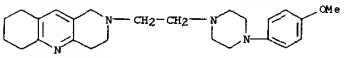
RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-



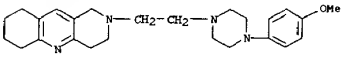
RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

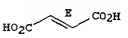
CRN 83082-29-5
CMF C25 H34 N4 O



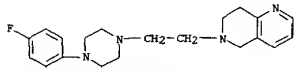
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

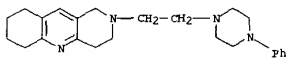
Double bond geometry as shown.



RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)



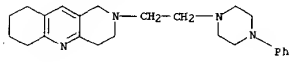
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

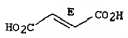
CRN 83082-23-9
CMF C24 H32 N4



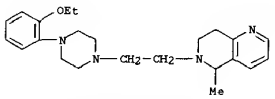
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

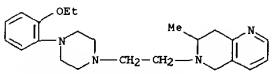
Double bond geometry as shown.



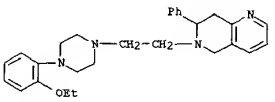
RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



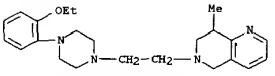
RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 83082-60-4 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-phenyl- (9CI) (CA INDEX NAME)



RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)

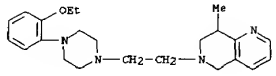


RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

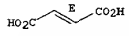
CRN 83082-61-5
CMF C23 H32 N4 O



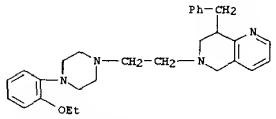
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-63-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

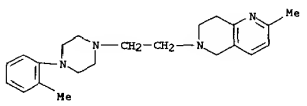


RN 83082-64-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-(phenylmethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

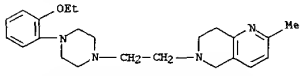
CM 1

CRN 83082-63-7
CMF C29 H36 N4 O

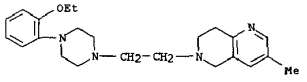
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



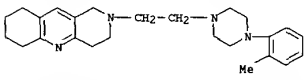
RN 83100-13-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 83100-17-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

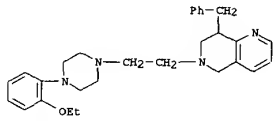


RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA

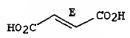
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



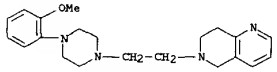
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

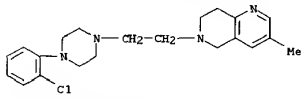
Double bond geometry as shown.



RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-01-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

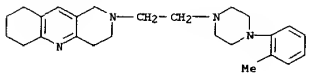


RN 83100-11-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
INDEX NAME)

CM 1

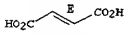
CRN 83100-19-0
CMF C25 H34 N4



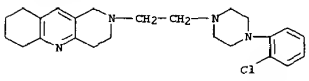
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

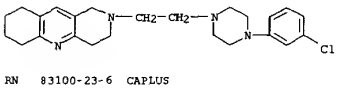
Double bond geometry as shown.



RN 83100-21-4 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

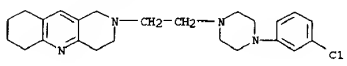


RN 83100-23-6 CAPLUS

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX
NAME)

CM 1

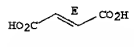
CRN 83100-22-5
CMF C24 H31 Cl N4



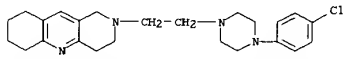
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX
NAME)

CM 1

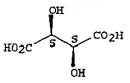
CRN 83100-24-7
CMF C24 H31 Cl N4

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

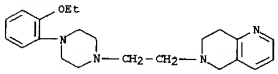
CM 2

CRN 133-37-9
CMF C4 H6 O6

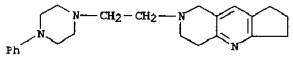
Relative stereochemistry.



RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



RN 83100-37-2 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

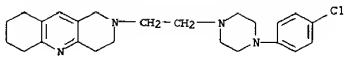


RN 83100-38-3 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-37-2
CMF C23 H30 N4

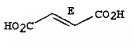
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



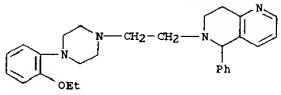
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



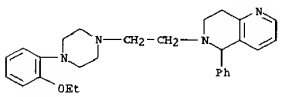
RN 83100-26-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)



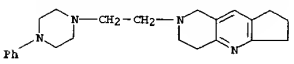
RN 83100-27-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

CRN 83100-26-9
CMF C28 H34 N4 O



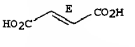
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



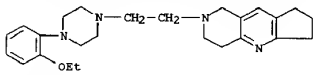
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



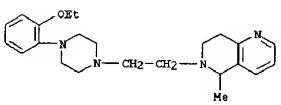
RN 83100-39-4 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-
piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)



RN 84414-63-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

CRN 83082-37-5
CMF C23 H32 N4 O

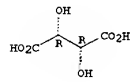


CM 2

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CRN 87-69-4
CMF C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.



L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:46453 CAPLUS
DOCUMENT NUMBER: 98:46453
TITLE: Buspirone analogs. 1. Structure-activity relationships in a series of N-aryl- and heteroarylpiperazine derivatives
AUTHOR(S): Yevich, J. P.; Temple, D. L., Jr.; New, J. S.; Taylor, Duncan P.; Riblet, L. A.
CORPORATE SOURCE: CNS Res.-Pharm. Res. Dev. Div., Bristol-Myers Co., Evansville, IN, 47721, USA
SOURCE: J. Med. Chem. (1983), 26(2), 194-203
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 98:46453
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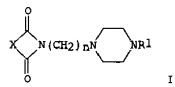


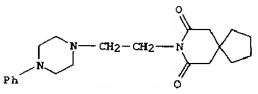
I

AB The title compds. I (X = substituted cyclic imide; R1 = substituted Ph, substituted pyridyl or substituted pyrimidinyl; n = 2-4) as the HCl salts were prepd. by the reaction of the appropriate piperazinebutanamine with the corresponding cyclic oxy compd. or by the reaction of a substituted piperazine with the corresponding cyclic imide. I and related analogs were tested in vitro for the binding affinities to rat brain membrane sites labeled with either the dopamine antagonist [3H]spiperone or the .alpha.1-adrenergic antagonist [3H]WB-4101 and in vivo for tranquilizing properties and induction of catalepsy. The azaspirodecanedione moiety affords the strongest affinity for dopaminergic binding sites and the most selectivity relative to .alpha.1-adrenergic blocking potential. Structure-activity relations are discussed.

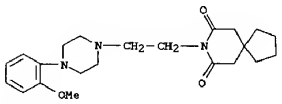
IT **21090-07-3 21102-94-3 21103-20-8 25024-93-5 25024-94-6 83928-69-2 83928-77-2 83928-78-3**
RL: BIOL (Biological study)
(anxiolytic and receptor binding activities of)

RN 21090-07-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

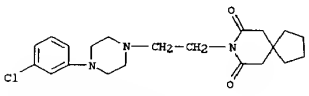
L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

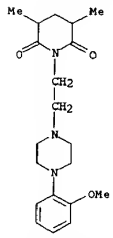


RN 21103-20-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

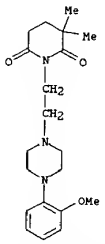


RN 25024-93-5 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

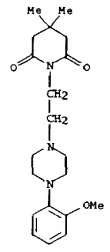
L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



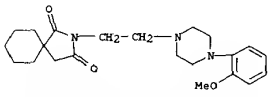
RN 25024-94-6 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)



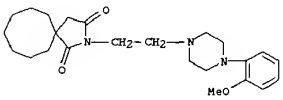
RN 83928-69-2 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



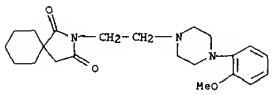
RN 83928-77-2 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83928-78-3 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

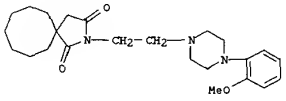


IT **83928-67-0 83928-68-1**
RL: BIOL (Biological study)
(pren. and anxiolytic and receptor binding activities of)
RN 83928-67-0 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

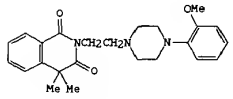
RN 83928-68-1 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 227 OF 263 CAPLUS COPYRIGHT 2002 ACS

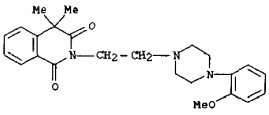
ACCESSION NUMBER: 1983:27864 CAPLUS
DOCUMENT NUMBER: 98:27864
TITLE: Possible role of central .alpha.1-adrenoceptors in the control of the autonomic nervous system in normotensive and spontaneously hypertensive rats
AUTHOR(S): Huchet, Anne Marie; Doursout, Marie Francoise; Chelly, Jacques; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med. Broussais-Hotel Dieu, Paris, 75006, Fr.
SOURCE: Eur. J. Pharmacol. (1982), 85(2), 239-42
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The cardiovascular effects of AR-C 239 (I) **[67339-62-2]**, a new and selective .alpha.1-adrenoceptor blocking drug, were studied in normotensive and spontaneously hypertensive rats (SHR). AR-C 239 (300 .mu.g/kg, i.v.) did not change the heart rate in control (without pretreatment) and bilaterally vagotomized normotensive rats, but induced significant bradycardia in rats pretreated with a .beta.-adrenoceptor blocking drug. The bradycardic effect was inhibited by atropine or bilateral vagotomy. In SHR, the administration of AR-C 239 reduced heart rate in the control, bilaterally vagotomized and .beta.-blocked rats. Blood pressure was decreased in the same way in the 2 rat strains. Apparently, central .alpha.1-adrenoceptors could participate in the control of vagal tone in normotensive and SH rats, and of sympathetic activity in the SHR only.

IT **67339-62-2**
RL: BIOL (Biological study)
(nervous system response to, in hypertension, adrenoceptors in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

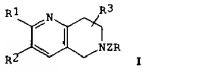


L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:544876 CAPLUS
DOCUMENT NUMBER: 97:144876
TITLE: 5,6,7,8-Tetrahydro-1,6-naphthyridine derivatives
INVENTOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Ishihawa, Michio; Miyazaki, Hiroshi
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd. , Japan
SOURCE: Ger. Offen., 109 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

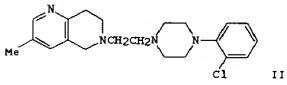
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3143016	A1	19820527	OE 1981-3143016	19811029
JP 57075983	A2	19820512	JP 1980-150719	19801029
JP 58057379	A2	19830405	JP 1981-154863	19811001
SE 8106359	A	19820430	SE 1981-6359	19811028
GB 2087390	A	19820526	GB 1981-32554	19811029
GB 2087390	B2	19840613		
ES 516935	A1	19840216	ES 1982-516935	19821015

PRIORITY APPLN. INFO.: JP 1980-150719 19801029
JP 1981-154863 19811001

GI



I

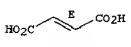


II

AB The title naphthyridines I [R = dialkylamino, pyrrolidinyl, hydroxyphenylpiperidinyl, 1-morpholinyl, 4-alkyl-, 4-benzyl-, 4-pyridyl-, or 4-(un)substituted-phenylpiperazinyl; R1, R2 = alkyl, R1R2 = C2-5 alkylene; R3 = H, alkyl, Bz, R4C6H4 (R4 = H, halo, alkyl, alkoxy); Z = C2-4 alkylene], useful in treatment of vertigo and as muscle relaxants (data tabulated), were prepd. Alkylating 5,6,7,8-tetrahydro-3-methyl-1,6-naphthyridine with 1-(2-chloroethyl)-4-(2-chlorophenyl)piperazine-2HCl in EtOH-NEt3 gave 41% naphthyridine II, which was converted to its difumarate.

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

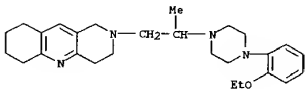
Double bond geometry as shown.



IT **83081-60-1**
RL: RCT (Reactant)
(nystagmus inhibitory activity of)
RN 83081-60-1 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

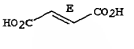
CRN 83081-59-8
CMF C27 H38 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

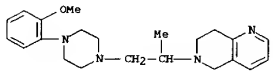


IT **83082-28-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and muscle relaxant activity of)
RN 83082-28-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT **83081-74-7 83082-18-2**
RL: RCT (Reactant)
(muscle relaxant activity of)
RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

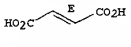
CRN 83081-73-6
CMF C22 H30 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

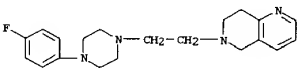
Double bond geometry as shown.



RN 83082-18-2 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-17-1
CMF C20 H25 F N4

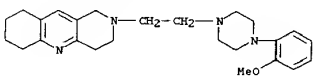


CM 2

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

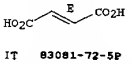
CRN 83082-27-3
CMF C25 H34 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

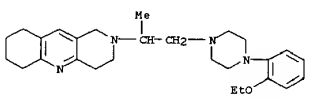
Double bond geometry as shown.



IT **83081-72-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nystagmus inhibitory activity of)
RN 83081-72-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83081-71-4
CMF C27 H38 N4 O

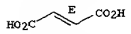


CM 2

CRN 110-17-8
CMF C4 H4 O4

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CDES 2:E

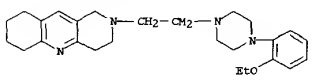
Double bond geometry as shown.



IT **83081-78-1P 83082-67-1P 83100-04-3P**
83100-12-3P 83100-14-5P 83100-18-9P
83100-36-1P 83100-40-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nystagmus inhibitory and muscle relaxant activity of)
RN 83081-78-1 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX
NAME)

CM 1

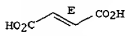
CRN 83081-77-0
CMF C26 H36 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

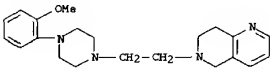


RN 83082-67-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-65-9
CMF C21 H28 N4 O

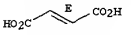
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

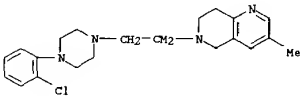
Double bond geometry as shown.



RN 83100-04-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9Cl) (CA INDEX NAME)

CM 1

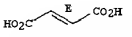
CRN 83100-01-0
CMF C21 H27 Cl N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

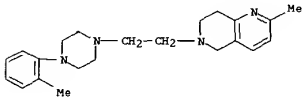


RN 83100-12-3 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

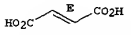
CRN 83100-11-2
CMF C22 H30 N4



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

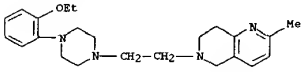
Double bond geometry as shown.



RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

CRN 83100-13-4
CMF C23 H32 N4 O

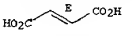


CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

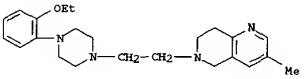
Double bond geometry as shown.



RN 83100-18-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

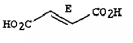
CRN 83100-17-8
CMF C23 H32 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

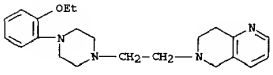
Double bond geometry as shown.



RN 83100-36-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

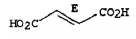
CRN 83100-35-0
CMF C22 H30 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

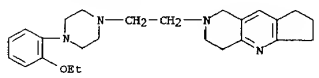
Double bond geometry as shown.



RN 83100-40-7 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

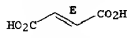
CRN 83100-39-4
CMF C25 H34 N4 O



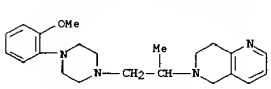
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

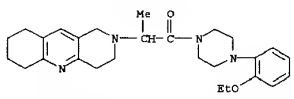
Double bond geometry as shown.

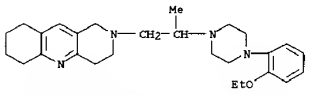


IT **83099-95-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 83099-95-0 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

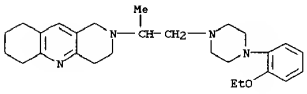


IT **83081-59-8P 83081-71-4P 83081-73-6P**
83081-74-7P 83081-76-9P 83081-77-0P
83082-17-1P 83082-23-9P 83082-24-0P
83082-27-3P 83082-29-5P 83082-30-8P
83082-37-5P 83082-38-6P 83082-59-1P
83082-60-4P 83082-61-5P 83082-62-6P
83082-63-7P 83082-64-8P 83082-65-9P
83100-01-0P 83100-11-2P 83100-13-4P
83100-17-8P 83100-19-0P 83100-20-3P
83100-21-4P 83100-22-5P 83100-23-6P
83100-24-7P 83100-25-8P 83100-26-9P
83100-27-0P 83100-35-0P 83100-37-2P
83100-38-3P 83100-39-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 83081-59-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)





RN 83081-71-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



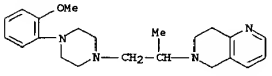
RN 83081-73-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-

piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

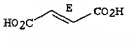
CRN 83081-73-6
CMF C22 H30 N4 O



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

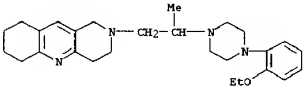
Double bond geometry as shown.



RN 83081-76-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

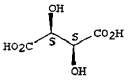
CRN 83081-59-8
CMF C27 H38 N4 O



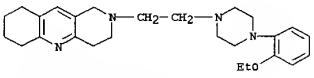
CM 2

CRN 133-37-9
CMF C4 H6 O6

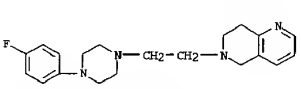
Relative stereochemistry.



RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

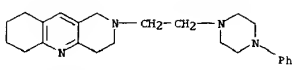


RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

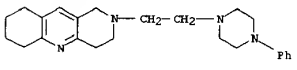
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

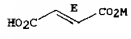
CRN 83082-23-9
CMF C24 H32 N4



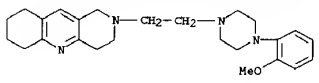
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

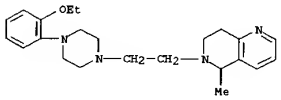


RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-5-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

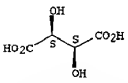
CRN 83082-37-5
CMF C23 H32 N4 O



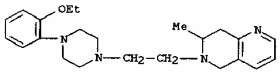
CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.

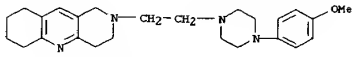


RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



RN 83082-60-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-phenyl- (9CI) (CA INDEX NAME)

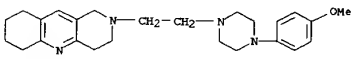
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

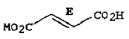
CRN 83082-29-5
CMF C25 H34 N4 O



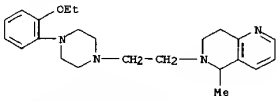
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

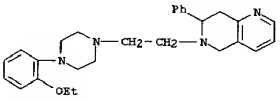


RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)

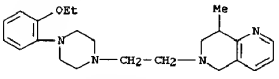


RN 83082-38-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



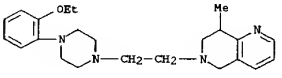
RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

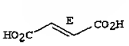
CRN 83082-61-5
CMF C23 H32 N4 O



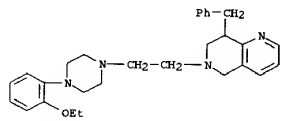
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



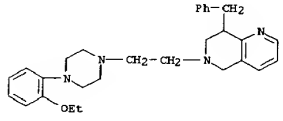
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 83082-63-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-[2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 83082-64-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-(phenylmethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX
NAME)

CM 1

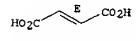
CRN 83082-63-7
CMF C29 H36 N4 O



CM 2

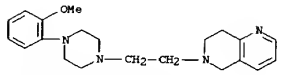
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

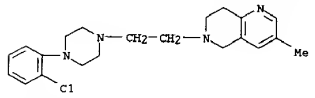


RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-

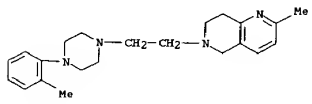
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



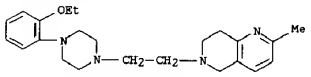
RN 83100-01-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-11-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

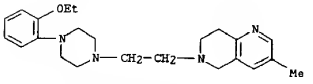


RN 83100-13-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl- (9CI) (CA INDEX NAME)

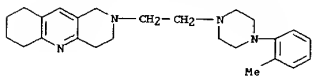


RN 83100-17-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



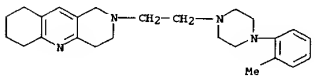
RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

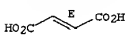
CRN 83100-19-0
CMF C25 H34 N4



CM 2

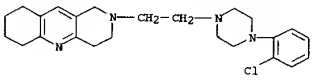
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

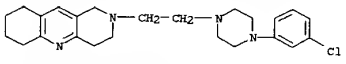


L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 83100-21-4 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



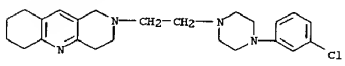
RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-23-6 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

CRN 83100-22-5
CMF C24 H31 Cl N4

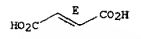


CM 2

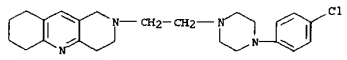
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



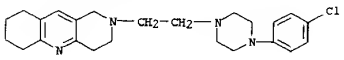
RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CM 1

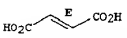
CRN 83100-24-7
CMF C24 H31 Cl N4



CM 2

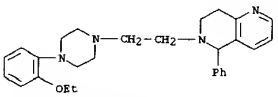
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83100-26-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)

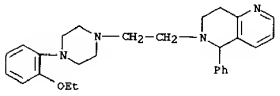
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83100-27-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA
INDEX NAME)

CM 1

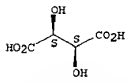
CRN 83100-26-9
CMF C28 H34 N4 O



CM 2

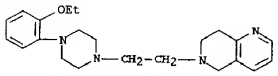
CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.

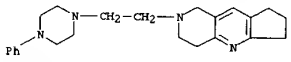


RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



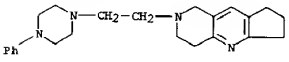
RN 83100-37-2 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83100-38-3 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

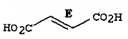
CRN 83100-37-2
CMF C23 H30 N4



CM 2

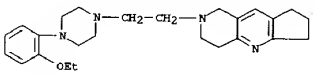
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



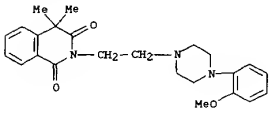
RN 83100-39-4 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-
piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

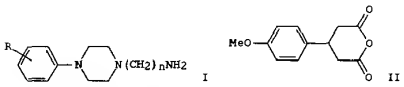


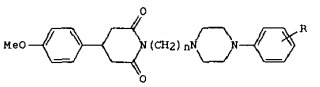
L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:538576 CAPLUS
DOCUMENT NUMBER: 97:138576
TITLE: GTP regulates binding of agonists to .alpha.2-adrenergic receptors in human platelets
AUTHOR(S): Brodde, O. E.; Hardung, A.; Ebel, H.; Bock, K. D.
CORPORATE SOURCE: Med. Klin. Poliklin., Univ. Essen, Essen, D-4300, Fed. Rep. Ger.
SOURCE: Arch. Int. Pharmacodyn. Ther. (1982), 258(2), 193-207
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potent .alpha.2-adrenergic receptor antagonist 3H-labeled yohimbine [146-48-5] was used to characterize .alpha.-adrenergic receptors in human platelet membranes. Binding of [3H]yohimbine at 25 .degree. was rapid (t1/2 = 3 min), readily reversible (t1/2 = 5.5 min), saturable with 221 fmoles bound/mg protein, and of high affinity (KD = 1.97 nM). Inhibition of binding by .alpha.-adrenergic antagonists showed monophasic displacement curves with Hill-coeffs. of approx. 1.0. The rank order of potency was: rauwolscine [131-03-3] .gtoreq. yohimbine > phentolamine [50-60-2] > phenoxybenzamine [59-96-1] > AR-C 239 **[67339-62-2]** .gtoreq. corynanthine [483-10-3] > prazosin [19216-56-9], indicating that the .alpha.-adrenergic receptor in human platelets is of the .alpha.2-subtype. On the contrary, agonist (clonidine [4205-90-7], guanfacine [29110-47-2], (-)-.alpha.-methylnoradrenaline [829-74-3], (-)-noradrenaline [51-41-2] and (-)-adrenaline [51-43-4]) displacement curves were shallow with Hill-coeffs. of approx. 0.7. Non-linear regression anal. showed that agonists bind to 2 affinity states of the .alpha.2-adrenergic receptor, a high and a low affinity state. In the presence of GTP [86-01-1] (10-14 M) agonist concn.-inhibition curves were shifted to the right to lower affinities and Hill-coeffs. increased up to 1.0. KI values for inhibition of binding in the presence of GTP were in the same range as those for low affinity state in the absence of GTP. Apparently, GTP regulates binding of .alpha.2-adrenergic agonists at the human .alpha.2-adrenergic receptor.
IT **67339-62-2**
RL: PROC (Process)
(binding of, to .alpha.-adrenergic receptors of blood platelets of humans)

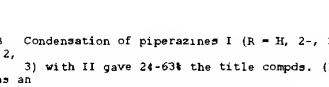
L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:550591 CAPLUS
DOCUMENT NUMBER: 95:150591
TITLE: Synthesis and pharmacology of 1-(4-aryl-1-piperazinylalkyl)-4-(4-methoxyphenyl)piperidine-2,6-diones: tranquilizers
AUTHOR(S): Samant, S. D.; Kulkarni, R. A.
CORPORATE SOURCE: Dep. Chem., Ramnarain Ruia Coll., Bombay, 400 019, India
SOURCE: J. Indian Chem. Soc. (1981), 58(7), 692-4
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

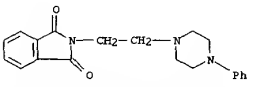




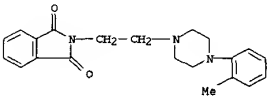


AB Condensation of piperazines I (R = H, 2-, 3-, 4-Me, 2-, 3-, 4-Cl; n = 2, 3) with II gave 24-63% the title compds. (III). III (R = H, n = 2) has an amphetamine antagonist ED50 of 38 mg/kg s.c. in mice.
IT **75000-24-7 75000-25-8 75000-26-9 75000-27-0 75000-28-1 75000-29-2 75000-30-5**
RL: RCT (Reactant)
(hydrolysis of)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

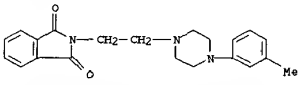
L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



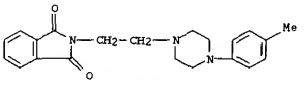
RN 75000-25-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



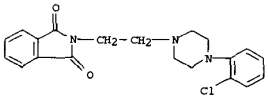
RN 75000-26-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



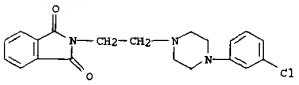
RN 75000-27-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



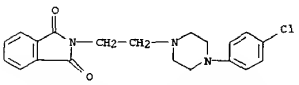
RN 75000-28-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 75000-29-2 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

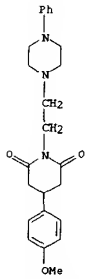


RN 75000-30-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT **79322-94-4P 79322-95-5P 79322-96-6P 79322-97-7P 79322-98-8P 79322-99-9P 79323-00-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and central nervous system depressant activity of)

RN 79322-94-4 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 79322-95-5 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

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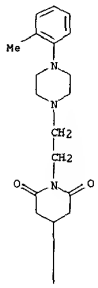
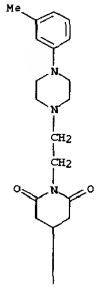


PAGE 2-A

RN 79322-96-6 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

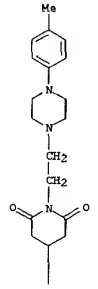
PAGE 1-A



PAGE 2-A

RN 79322-97-7 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

RN 79322-98-8 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

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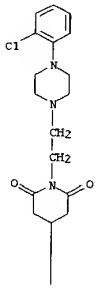
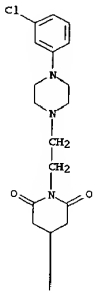


PAGE 2-A

RN 79322-99-9 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A

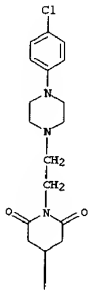


PAGE 2-A

RN 79323-00-5 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

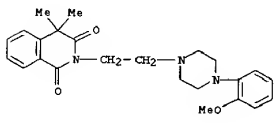
L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A



PAGE 2-A

L14 ANSWER 231 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:490956 CAPLUS
DOCUMENT NUMBER: 95:90956
TITLE: Role of .alpha.1- and .alpha.2-adrenoceptors in the modulation of the baroreflex vagal bradycardia
AUTHOR(S): Huchet, Anne Marie; Chelly, Jacques; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.
SOURCE: Eur. J. Pharmacol. (1981), 71(4), 455-61
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Yohimbine-HCl [65-19-0] (100 .mu.g/kg), an .alpha.2-adrenoceptor blocking agent when injected into the vertebral artery of anesthetized dogs decreased the vagally mediated bradycardia induced by carotid sinus nerve stimulation. Intracisternal administration of phenylephrine-HCl [61-76-7] (30 .mu.g/kg) an .alpha.1-adrenoceptor agonist decreased, whereas AR-C 239-HCl [**78448-19-8**] (5 .mu.g/kg) and prazosin-HCl [19237-84-4] (5 .mu.g/kg) 2 potent .alpha.1-adrenoceptor antagonists injected into the vertebral artery, potentiated the bradycardic response. These results suggest, the presence of 2 types of .alpha.-adrenoceptors to modulate the baroreceptor pathway: .alpha.1-adrenoceptors inhibit and .alpha.2-adrenoceptors facilities the transmission of baroreceptor impulses.
IT **78448-19-8**
RL: BIOL (Biological study)
(bradycardia response to, baroreflex in relation to)
RN 78448-19-8 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



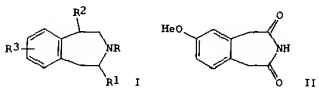
● x HCl

L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:47157 CAPLUS
DOCUMENT NUMBER: 94:47157
TITLE: Substituted 1,2,4,5-tetrahydro-3H,3 benzazepines
INVENTOR(S): Shetty, Bola V.
PATENT ASSIGNEE(S): Pennwalt Corp., USA
SOURCE: U.S., 30 pp. Division of U.S. Ser. No. 747,151, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4210749	A	19800701	US 1979-41574	19790521
US 4233217	A	19801111	US 1979-41575	19790521

PRIORITY APPLN. INFO.: US 1968-711897 19680311
US 1972-241091 19720404
US 1974-523092 19741112
US 1976-747151 19761203

GI



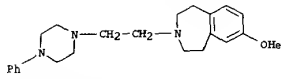
I II

AB Benzazepines I (R = H, alkyl, alkenyl, aralkenyl, cycloalkylalkyl, aralkyl, heterocyclic alkyl; R1 = H, alkyl, Ph, phenylalkyl; R2 = H, alkyl; R3 = H, alkoxy, alkyl, halo, NO2, HO), useful as analgesics and narcotic antagonists, were prepd. Thus, treatment of 3,4-(NCCH2)2C6H3OMe with HBr-AcOH followed by heating at 85.degree. with NaOAc gave II, which was treated with BH3 to give I (R = R1 = R2 = H, R3 = HeO) (III). Refluxing III in 48% HBr gave I (R = R1 = R2 = H, R3 = HO).

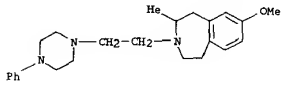
IT **36134-35-7P 76216-21-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pharmacol. of)

RN 36134-35-7 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



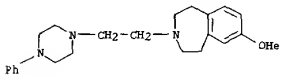
RN 76216-21-2 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

1T **36134-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



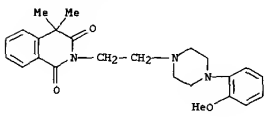
●2 HCl

L14 ANSWER 233 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:44562 CAPLUS
DOCUMENT NUMBER: 94:44562
TITLE: Identification of .alpha.2-adrenergic receptors in human fat cell membranes by [3H]-clonidine binding
AUTHOR(S): Berlan, Michel; Lafontan, Max
CORPORATE SOURCE: Lab. Physiol. Appl. Pharmacol. Med., Fac. Med., Toulouse, F-31000, Fr.
SOURCE: Eur. J. Pharmacol. (1980), 67(4), 481-4
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB [3H]clonidine bound to membrane sites of human fat cells, which have the characteristics of .alpha.2-adrenoceptors. Specific binding was rapid, reversible, and saturable. [3H]clonidine binding was of high affinity with a KD of 3.9 nM and with a maximal occupancy of 348 fmol/mg protein. The correlation between .alpha.-adrenergic agonist or antagonist affinities for the membrane [3H]clonidine binding site with their physiol. potencies demonstrates the usefulness of the human fat cell as a model for investigating postsynaptic .alpha.2-adrenoceptor properties and regulation.

IT **67339-62-2**
RL: BIOL (Biological study)
(adrenergic receptors of adipocyte cell membrane binding of, clonidine competition with)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

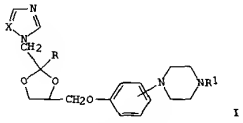


L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:620771 CAPLUS
DOCUMENT NUMBER: 93:220771
TITLE: Fungicidal and bactericidal[4-(piperazin-1-ylphenyloxymethyl)-1,3-dioxolan-2-ylmethyl]-1H-imidazoles and -1H-1,2,4-triazole derivatives
INVENTOR(S): Heeres, Jan; Hostmans, Joseph
PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
SOURCE: Eur. Pat. Appl., 68 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 6722	A1	19800109	EP 1979-301151	19790615
EP 6722	B1	19840905		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 9227	E	19840915	AT 1979-301151	19790615
JP 63045389	B4	19880909	JP 1979-82739	19790702
US 4503055	A	19850305	US 1981-306267	19810928

PRIORITY APPLN. INFO.: US 1978-921380 19780703
US 1979-23807 19790326
EP 1979-301151 19790615

GI



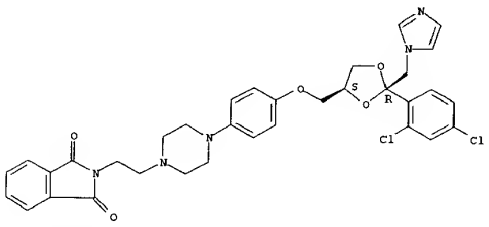
I

AB Approx. 100 title compds. I [R = (substituted) Ph, thienyl, or halothienyl; R1 = alkylsulfonyl, CF3SO2, alkyl or alkenyl substituted by CN, (substituted) NH2, N heterocyclyl, aryl, or aryloxy, or R1 = CnH2nC(X1)R2, where R2 = H, (substituted) alkyl, alkoxy, (substituted) NH2, etc., X1 = O or S, n = 0-6; X = CH or N] were prepd. by several procedures. Thus, treatment of cis-1-[4-[[2-(2,4-dichlorphenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine with ClCH2CO2Et and K2CO3 in Me2SO gave cis-I (R = 2,4-Cl2C6H3, R1 = CO2CH2CO2Et, X = CH), which had ED50 2.5 mg/kg (p.o) for vaginal candidosis in rats and ED50 31 mg/kg (in feed) for crop candidosis in turkeys.

IT **75049-24-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 75049-24-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]ethyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



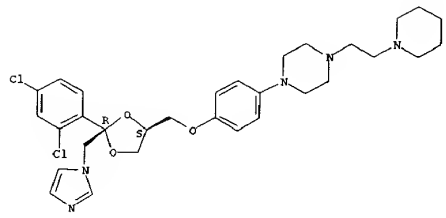
IT **75049-53-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 75049-53-5 CAPLUS
CN Piperazine,
1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-4-[2-(1-piperidinyl)ethyl]-, cis-, ethanedioate (1:3) (9CI) (CA INDEX NAME)

CM 1

CRN 75049-52-4
CMF C31 H39 C12 N5 O3
CDES 2:CIS

Relative stereochemistry.

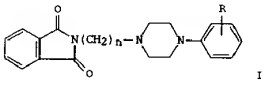
L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

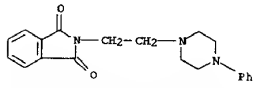
CRN 144-62-7
CMF C2 H2 O4

L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:550208 CAPLUS
DOCUMENT NUMBER: 93:150208
TITLE: Synthesis and pharmacology of N-(N4-aryl-N1-piperazinylalkyl)phthalimides: CNS depressants
AUTHOR(S): Samant, S. D.; Kulkarni, R. A.
CORPORATE SOURCE: Chem. Dep., Ramnarain Ruia Coll., Bombay, 400 019, India
SOURCE: J. Indian Chem. Soc. (1979), 56(10), 1002-5
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



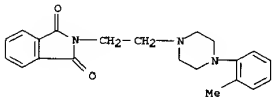
I

AB Twenty one phthalimides I (n = 1, 2, 3; R = H, Me, Cl) were prepd. by Mannich reaction of phthalimides with piperazines in presence of HCHO or by reaction of bromoalkylphthalimides with arylpiperazines. These compds. were inactive as central nervous system depressants. I exhibited a tranquilizing effect on test animals and were non-toxic.
IT **75000-24-7P 75000-25-8P 75000-26-9P**
75000-27-0P 75000-28-1P 75000-29-2P
75000-30-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tranquilizing activity of)
RN 75000-24-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
(CA INDEX NAME)

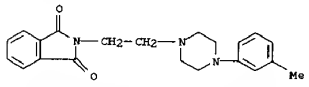


RN 75000-25-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

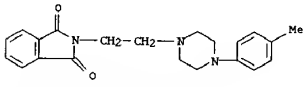
L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



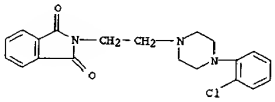
RN 75000-26-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



RN 75000-27-0 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

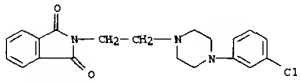


RN 75000-28-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

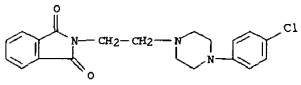


RN 75000-29-2 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-

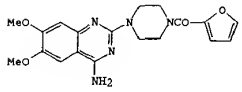
L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(9CI) (CA INDEX NAME)



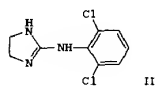
RN 75000-30-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



L14 ANSWER 236 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:525440 CAPLUS
DOCUMENT NUMBER: 93:125440
TITLE: 3H-Prazosin binds specifically to '.alpha.1'-adrenoceptors in rat brain
AUTHOR(S): Miach, Peter J.; Dausse, Jean Pierre; Cardot, Alain; Meyer, Philippe
CORPORATE SOURCE: Res. Unit, Hop. Necker, Paris, F-75015, Fr.
SOURCE: Naunyn-Schmiedeberg's Arch. Pharmacol. (1980), 312(1), 23-6
CODEN: NSAPCC; ISSN: 0028-1298
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



1



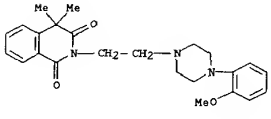
II

AB 3H-Labeled prazosin (I) [19216-56-9] was used to label biochem. central .alpha.-adrenoceptors. In rat brain membranes prazosin-3H bound specifically in a rapid, reversible and saturable manner to a single class of high affinity sites. The relative order of potencies for inhibition of prazosin-3H binding was WB4101 [2170-58-3] > ARC 239 [**67339-62-2**] > phentolamine [50-60-2] .mchgt. piperoxane [59-39-2] > yohimbine [146-48-5] which is a characteristic of the .alpha.1 type of adrenoceptors. In contrast, the relative order of potencies for inhibition of 3H-labeled clonidine (II) [4205-90-7] binding was yohimbine > piperoxane > WB4101 > ARC239 > prazosin which is a characteristic of the .alpha.2 type of adrenoceptors. Apparently, prazosin-3H binds to central .alpha.1-receptors and clonidine-3H binds to .alpha.2-receptors indicating the presence of two classes of .alpha.-adrenoceptors in rat brain membranes.

IT **67339-62-2**
RL: BIOL (Biological study)
(.alpha.-adrenergic receptors interaction with, in brain)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

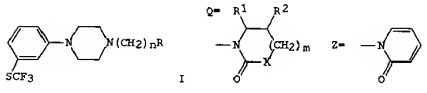
L14 ANSWER 236 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:514564 CAPLUS
DOCUMENT NUMBER: 93:114564
TITLE: 1-Substituted alkyl-4-(3-trifluoromethylthiophenyl)piperazines
INVENTOR(S): Najer, Henry; Manoury, Philippe; Kaplan, Jean Pierre
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2023594	A	19800103	GB 1979-21307	19790619
GB 2023594	B2	19821013		
FR 2429216	A1	19800118	FR 1978-18352	19780620
FR 2429216	B1	19801107		
FR 2429212	A1	19800118	FR 1978-18351	19780620
FR 2429212	B1	19801107		
CA 1124238	A1	19820525	CA 1979-329703	19790613
DK 7902510	A	19791221	DK 1979-2510	19790615
FI 7901926	A	19791221	FI 1979-1926	19790615
AU 7948112	A1	19800207	AU 1979-48112	19790615
AU 521110	B2	19820318		
US 4242343	A	19801230	US 1979-48814	19790615
NO 7902020	A	19791221	NO 1979-2020	19790618
ES 481632	A1	19800216	ES 1979-481632	19790618
BE 877099	A1	19791219	BE 1979-195839	19790619
SE 7905402	A	19791221	SE 1979-5402	19790619
DE 2924681	A1	19800110	DE 1979-2924681	19790619
JP 55007274	A2	19800119	JP 1979-77489	19790619
ZA 7903070	A	19800730	ZA 1979-3070	19790620
PRIORITY APPLN. INFO.:			FR 1978-18351	19780620
			FR 1978-18352	19780620

GI



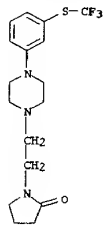
I

AB The prepn. of the title compds. I [n = 1, 2, 3; R1 = Q (R1 = R2 = H; R1R2 = benzo; X = O, S, NH, alkylimino, CH2; m = 0, 1), Z, 2-tetrahydrofuryl, CH2SR3 (R3 = H, alkyl, acyl), C1-8 alkoxymethyl] and I acid addn. salts is

L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
described. Thus, I (n = 2, R = Q, R1R2 = benzo, X = NMe, m = O) was prepd. by heating 4-(3-trifluoromethylthiophenyl)piperazine with powd. K2CO3, KI, and 1-(.beta.-chloroethyl)-3-methylbenzimidazolidin-2-one in PhMe at reflux under N for 16 h. I are useful for the treatment of anxiety and of depression. Their activity was assessed orally in mice. LD50 values for I in mice were 75-230 mg/kg for i.p. administration (48 h) and 250-1000 mg/kg for oral administration (7 days).

IT **74025-63-1P 74025-64-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as tranquilizer and antidepressant)

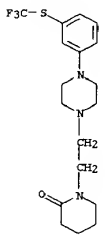
RN 74025-63-1 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 74025-64-2 CAPLUS
CN 2-Piperidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

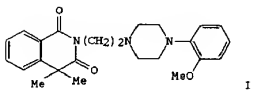
L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●x HCl

L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:437174 CAPLUS
DOCUMENT NUMBER: 93:37174
TITLE: Pharmacological properties of AR-C239, 2-[2-[4(O-methoxyphenyl)-piperazine-1-yl]ethyl]4,4-dimethyl-1,3(2H-4H) isoquinolinedione, a new .alpha.-adrenoceptor blocking drug
AUTHOR(S): Mouille, Paule; Huchet, Anne Marie; Chelly, Jacques; Lucet, Bernadette; Doursout, Marie Francoise; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.
SOURCE: J. Cardiovasc. Pharmacol. (1980), 2(2), 175-91
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



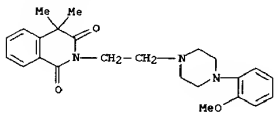
I

AB In pentobarbital-treated dogs and rats, AR-C239 (I) [**67339-62-2**] competitively antagonized pressor responses to adrenaline and inhibited pressor responses to noradrenaline, phenylephrine, tyramine, and dimethylphenylpiperazinium. Injected i.v. into closed-chest dogs, AR-C239 (3-50 .mu.g/kg) induced a progressive fall in blood pressure, heart rate, and sympathetic nerve activity. The drug appears to be devoid of direct vasodilator action, and the fall in blood pressure results from the peripheral .alpha.-blockade. AR-C239 did not change the tachycardia induced by stimulation of the cardiac nerve in dogs and, at least in this prepn., seems to be a specific .alpha.1-adrenoceptor blocking drug. When administered into the cisterna magna of dogs, AR-C239 did not have any centrally mediated cardiovascular actions and failed to block the inhibitor effects of clonidine on blood pressure and heart rate. AR-C239 did not have any centrally mediated cardiovascular actions and failed to block the inhibitory effects of clonidine on blood pressure and heart rate. AR-C239 did not modify the functioning of the baroreflex arc. Due to its specificity for .alpha.1-adrenoceptors, AR-C239 may be useful for characterizing .alpha.-adrenoceptors.

L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

IT **67339-62-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of)

RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

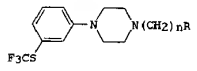


L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:426462 CAPLUS
DOCUMENT NUMBER: 93:26462
TITLE: Phenylpiperazine derivatives
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Neth. Appl., 9 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 7904755	A	19791227	NL 1979-4755	19790619
FR 2429216	A1	19800118	FR 1978-18352	19780620
FR 2429216	B1	19801107		
FR 2429212	A1	19800118	FR 1978-18351	19780620
FR 2429212	B1	19801107		
CA 1124238	A1	19820525	CA 1979-329703	19790613
DK 7902510	A	19791221	DK 1979-2510	19790615
FI 7901926	A	19791221	FI 1979-1926	19790615
AU 7948112	A1	19800207	AU 1979-48112	19790615
AU 521110	B2	19820318		
US 4242343	A	19801230	US 1979-48814	19790615
NO 7902020	A	19791221	NO 1979-2020	19790618
ES 481632	A1	19800216	ES 1979-481632	19790618
BE 877099	A1	19791219	BE 1979-195839	19790619
SE 7905402	A	19791221	SE 1979-5402	19790619
DE 2924681	A1	19800110	DE 1979-2924681	19790619
JP 55007274	A2	19800119	JP 1979-77489	19790619
ZA 7903070	A	19800730	ZA 1979-3070	19790620

PRIORITY APPLN. INFO.: FR 1978-18351 19780620
FR 1978-18352 19780620

GI



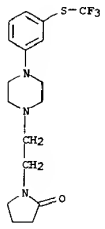
I

AB Tranquilizing (no data) piperazines I (n = 1-3; R = heterocyclic amino) were prepd. Thus, 4-(3-trifluoromethylthiophenyl)piperazine was treated with 1-(2-chloroethyl)-2-pyridone to give I (n = 2, R = 2-oxo-1-pyridyl).

IT **74025-63-1P 74025-64-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

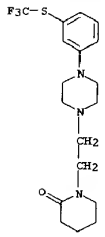
RN 74025-63-1 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



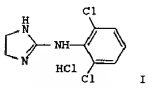
●x HCl

RN 74025-64-2 CAPLUS
CN 2-Piperidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

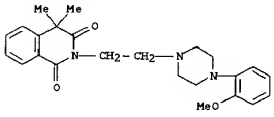
L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:174421 CAPLUS
DOCUMENT NUMBER: 92:174421
TITLE: Interactions between clonidine and .alpha.-adrenoceptor blocking drugs on the tachycardic response to stimulation of the cardiac nerve in dogs
AUTHOR(S): Mouille, Paule; Huchet, Anne Marie; Lucet, Bernadette; Chelly, Jacques; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharm., Fac. Med. Broussais, Paris, Fr.
SOURCE: J. Cardiovasc. Pharmacol. (1979), 1(5), 515-28
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



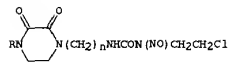
I

AB In pentobarbital-treated dogs clonidine-HCl (I) [4205-91-8] (10 .mu.g/kg) reduced the increase in heart rate caused by elec. stimulation of the cardiac nerve (1-10 Hz). Yohimbine-HCl [65-19-0] (0.3 mg/kg) and phentolamine-HCl [73-05-2] (1 mg/kg) potentiated the effects of nerve stimulation and antagonized the inhibitory effects of I. Piperoxan-HCl [135-87-5] (1 mg/kg) increased the response to nerve stimulation but antagonized the effects of I only at the lowest frequency of stimulation. Thymoxamine-HCl [964-52-3] (1 mg/kg) and prazosin-HCl [19237-84-4] at high doses (1 mg/kg) also antagonized the effects of I but failed to increase the pos. chronotropic response to stimulation of the cardiac nerve. AR-C239 [**67339-62-2**], a new and potent .alpha.-adrenoceptor blocking agent, changed neither the response to nerve stimulation nor the inhibitory effect of I. The effects of all these drugs were obsd. at doses which reduced or reversed the pressor response to adrenaline. Therefore, the results afford further evidence for a dissimilarity between postsynaptic and presynaptic .alpha.-adrenoceptors in the dog. In addn., they show that the failure of an .alpha.-adrenoceptor blocking compd. to increase the response to nerve stimulation does not necessarily indicate a lack of presynaptic .alpha.-adrenoceptor blockade.

L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT **67339-62-2**
RL: BIOL (Biological study)
(heart response to clonidine in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

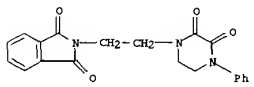


L14 ANSWER 241 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:611367 CAPLUS
DOCUMENT NUMBER: 91:211367
TITLE: Synthesis and physico-chemical properties of 1-(2-chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosourea
AUTHOR(S): Hori, Takako; Momonoi, Kaishu; Kiba, Yasuo; Yoshida,
Chosaku; Sakai, Hiroshi; Takeno, Ryuko; Ohashi, Toshinori; Kishimoto, Sumiko; Saikawa, Isamu
CORPORATE SOURCE: Res. Lab., Toyama Chem. Co., Ltd., Toyama, Japan
SOURCE: Yakugaku Zasshi (1979), 99(7), 730-7
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



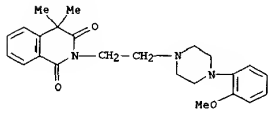
I

AB 1-(2-Chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosoureas I (R = H, C1-8 alkyl, Ph; n = 0-6) were prepd. by treating the dioxopiperazinylalkylamines with 4-O2NC6H4O2CN(NO)CH2CH2Cl on with ClCH2CH2NCO followed by nitrosation and their physico-chem. properties were examd. Along with an increase in n, the alkylating activity was reduced, the stability in aq. soln. at pH 7-8 was increased, and the NH proton of the NMR spectrum was shifted to a higher field. These properties were not related to R.
IT **71999-88-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrazinolysis of)
RN 71999-88-7 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[2-(2,3-dioxo-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1979:115517 CAPLUS
DOCUMENT NUMBER: 90:115517
TITLE: Biochemical evidence for presynaptic and postsynaptic
.alpha.-adrenoceptors in rat heart membranes: Positive homotropic cooperativity of presynaptic binding
AUTHOR(S): Guicheney, Pascale; Garay, Ricardo P.; Levy-Marchal,
Claire; Meyer, Philippe
CORPORATE SOURCE: Dep. Physiol. Pharmacol., Hop. Necker, Paris, Fr.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1978), 75(12), 6285-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In crude rat cardiac membrane prepns., dihydroergocryptine-3H (I) appeared to bind 2 classes of sites with limited capacity, differing in their specificities and their affinities. The 1st class of binding sites interacted preferentially with the postsynaptic .alpha.-adrenoceptor blocker ARC 239 **(67339-62-2)**, as expected for postsynaptic .alpha.-adrenoceptors. The binding of I to these receptors followed the law of mass action, with a high affinity for I apparent dissocn. const. (Kd) at 25.degree. = 1.67 nM). Postsynaptic satg. levels of I were necessary to occupy the 2nd class of binding sites. These sites exhibit a preferential affinity for presynaptic ligands such as clonidine [4205-90-7] and yohimbine-HCl [65-19-0], as expected for presynaptic .alpha.-adrenergic receptors. This presynaptic binding showed a markedly pos. homotropic cooperativity (Hill n = 2.88) with initial and final Kds of 23 and 0.83 nM, resp. Free energy of interaction between sites was of the order of 2 kcal (8.36 kJ)/mol of sites. These characteristics provide a rational mol. basis for the functional role of presynaptic .alpha.-adrenoceptors that mediate the inhibition of norepinephrine release from nerve endings.
IT **67339-62-2**
RL: PROC (Process)
(heart membrane binding of)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

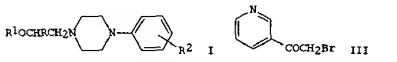
L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 243 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 197B:597598 CAPLUS
DOCUMENT NUMBER: 89:197598
TITLE: 1-Alkyl-substituted 4-phenylpiperazine derivatives
PATENT ASSIGNEE(S): MALESCI S.a.S. Istituto Farmacobiologico, Italy
SOURCE: Span., 29 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

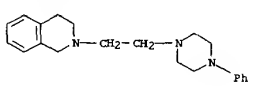
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 452530	A3	19780201	ES 1976-452530	19761019

GI



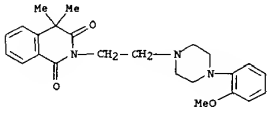
I III

AB 1-Alkyl-4-arylpiperazines I (R = pyridyl, 4-imidazolyl, 1,2,3,4-tetrahydro-2-isoquinolyl, 1,2,3,4-tetrahydro-2-methyl-3-isoquinolyl; R1 = alkyl, R2 = H, Cl, F, Me, MeO) were prepd. by treatment of RCOCH2Br with 1-phenylpiperazine (II) or its aryl-substituted derivs., followed by redn. with NaBH4 and O-alkylation. Thus, III.HBr was treated with II in MeOH-Et3N under N at 5-10.degree. and then at room temp. The mixt. was cooled to 0.degree., aq. NaBH4 added dropwise and the mixt. kept at room temp. for 1 h. The product (I; R = 3-pyridyl, R1 = R2 = H) in HCCl3 at 0.degree. was treated with HCl (g), SOCl2 in HCCl3, and MeOH to give I (R = 3-pyridyl, R1 = Me, R2 = H).
IT **58013-22-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 58013-22-2 CAPLUS
CN Isoquinoline, 1,2,3,4-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

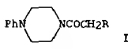


L14 ANSWER 243 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 244 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:500074 CAPLUS
DOCUMENT NUMBER: 89:100074
TITLE: Modifications of effects of cardiovascular nerve stimulation in the dog, by clonidine and several .alpha.-adrenolytics
AUTHOR(S): Mouille, Paule; Huchet, Anne-Marie; Lucet, Bernadette; Schmitt, Henri
CORPORATE SOURCE: Fac. med., Paris-Broussais-Hotel-Dieu, Paris, Fr.
SOURCE: C. R. Hebd. Seances Acad. Sci., Ser. D (1978), 286(19), 1399-402
CODEN: CHDDAT; ISSN: 0567-655X
DOCUMENT TYPE: Journal
LANGUAGE: French
AB In anesthetized dogs clonidine [4205-90-7] (0.01mg/kg, i. v.) reduced the tachycardia induced by stimulation of the cardiac nerve at low frequencies. Small doses of yohimbine [146-48-5] (0.3mg/kg, i. v.) or piperoxan [59-39-2] (0.3 mg/kg, i. v.) increased the effects of nerve stimulation and in addn. antagonized the inhibitory effects of clonidine . and reversed the pressor response to adrenaline [51-43-4]. Thymoxamine [54-32-0] (1 mg/kg, i. v.) and prazosin [19216-56-9] (1 mg/kg, i. v.) did not increase the effect of cardiac nerve stimulation, but reduced the effect of clonidine. ARC239 [**67339-62-2**] (0.05mg.kg-1) reversed the pressor response to adrenaline but even at high doses did not increase the effects of cardiac nerve stimulation or the effects of clonidine. Thus, pre- and post-synaptic .alpha.-adrenoceptors appear to be dissimilar.
IT **67339-62-2**
RL: BIOL (Biological study)
(tachycardia from cardiac nerve stimulation response to, quantity in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

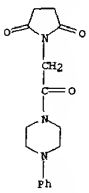


L14 ANSWER 245 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:50793 CAPLUS
DOCUMENT NUMBER: 88:50793
TITLE: Investigations on the piperazine series. New N-phenyl-piperazine acylate derivatives
AUTHOR(S): Zotta, V.; Popescu, Margareta; Missir, A.; Soare, Jeana; Capitanescu, Victoria; Fredescu, Viorica; Dicu, Elena; Neacsu, Maria
CORPORATE SOURCE: Lab. Chim. Farm., Fac. Farm., Bucharest, Rom.
SOURCE: Farmacia (Bucharest) (1977), 25(3), 129-35
CODEN: FRMBAZ
DOCUMENT TYPE: Journal
LANGUAGE: Romanian
GI



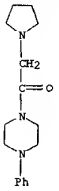
I

AB Nine piperazines I (R = 2,5-dioxopiperidino, piperidino, pyrrolidino, 2-pyridylamino, morpholino, etc.) were prepd. by treating I (R = Cl) with amines.
IT **65349-00-0P 65349-01-1P 65349-02-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 65349-00-0 CAPLUS
CN Piperazine, 1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

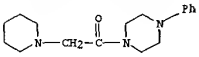


RN 65349-01-1 CAPLUS
CN Piperazine, 1-phenyl-4-(1-pyrrolidinylacetyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 245 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

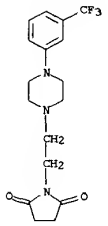


RN 65349-02-2 CAPLUS
CN Piperazine, 1-phenyl-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)



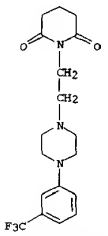
L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:495439 CAPLUS
DOCUMENT NUMBER: 87:95439
TITLE: Substituted trifluoromethyl phenyl piperazines as anorectic agents
AUTHOR(S): Cross, Peter E.; Dickinson, Roger P.; Halliwell, Geoffrey; Kemp, John E. G.
CORPORATE SOURCE: Pfizer Cent. Res., Pfizer Ltd., Sandwich/Kent, Engl.
SOURCE: Eur. J. Med. Chem. - Chim. Ther. (1977), 12(2), 173-6
CODEN: EJMCA5
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB In a series of trifluoromethyl phenyl piperazines possessing cyclo-imido
alkyl side chains (I) several compds. possessed good anorectic activity
with min. side effects on the central nervous system. The most potent no.
of the series was 1-(2-succinimidoethyl)-4-[4'-chloro-3-trifluoromethyl)phenyl]piperazine-HCl (II) [41213-05-2], which was prepd. by heating
1-[4'-chloro-3-(trifluoromethyl)phenyl]piperazine-HCl [63556-37-6] with 2-succinimidoethyl chloride [41212-96-8] in dry dimethylformamide in the presence of base.
IT **41212-97-9P 41212-99-1P 41213-05-2P**
63556-31-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and anorexic activity of)
RN 41212-97-9 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

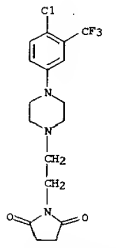
RN 41212-99-1 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

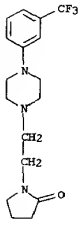
RN 41213-05-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[4-chloro-3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 63556-31-0 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

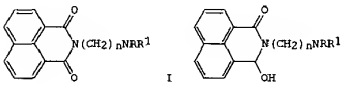


● HCl

L14 ANSWER 247 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1977:171284 CAPLUS
DOCUMENT NUMBER: 86:171284
TITLE: 2-[(Piperidinyl or tetrahydropyridinyl)-alkyl]-2,3-dihydro-3-hydroxy-1H-benz(de)isoquinolin-1-ones
INVENTOR(S): Wade, Peter C.; Vogt, Berthold Richard
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

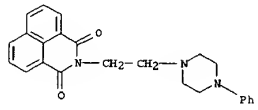
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4007191	A	19770208	US 1975-621939	19751014
GB 1567313	A	19800514	GB 1976-41959	19761008
CA 1068703	A1	19791224	CA 1976-263130	19761012
JP 52048674	A2	19770418	JP 1976-123369	19761014
DE 2646471	A1	19770421	DE 1976-2646471	19761014
FR 2327782	A1	19770513	FR 1976-30936	19761014
FR 2327782	B1	19781222		

PRIORITY APPLN. INFO.: US 1975-621939 19751014
GI



I II

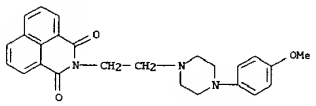
AB Benzisoquinolinediones I (n = 2-6, NRR1 = 4-substituted 1,2,3,6-tetrahydropyridino, piperidino, piperazino) were prepd. by treating naphthalic anhydride with H2N(CH2)nOH, tosylating, and treating
the ester with HNRR1 or by treating naphthalimide with Br(CH2)nBr and HNRR1. I were reduced with NaBH4 to give II which have antidepressant activity (no data).
IT **58895-65-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 58895-65-1 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

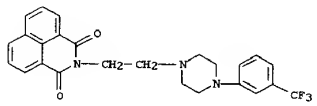
IT **58895-66-2P 58895-67-3P 58895-68-4P**
58895-69-5P 58895-70-8P 58895-71-9P
58895-76-4P 58895-78-6P 62614-87-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 58895-66-2 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



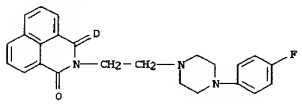
● 2 HCl

RN 58895-67-3 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



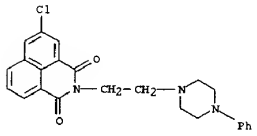
● HCl

RN 58895-71-9 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



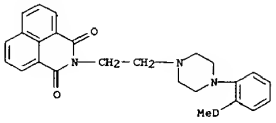
● HCl

RN 58895-76-4 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



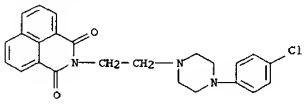
● HCl

RN 58895-78-6 CAPLUS



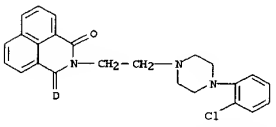
● 2 HCl

RN 58895-68-4 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



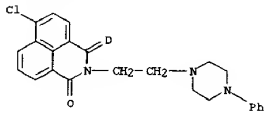
● HCl

RN 58895-69-5 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



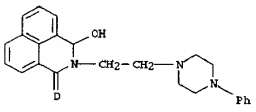
RN 58895-70-8 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione,
2-[2-[4-[3-(trifluoromethyl)phenyl]-
1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 6-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

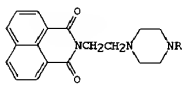
RN 62614-87-3 CAPLUS
CN 1H-Benz[de]isoquinolin-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:150664 CAPLUS
DOCUMENT NUMBER: 84:150664
TITLE: 2-[(Substituted-piperazinyl)alkyl]-1H-benz[de]isoquinoline-1,3(2H)-diones
INVENTOR(S): Wade, Peter C.; Vogt, Berthold R.
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3940397	A	19760224	US 1974-523293	19741113
CA 1058178	A1	19790710	CA 1975-239072	19751105
DE 2551062	A1	19760526	DE 1975-2551062	19751113
FR 2290903	A1	19760611	FR 1975-34615	19751113
FR 2290903	B1	19781110		
JP 51125293	A2	19761101	JP 1975-137115	19751113
PRIORITY APPLN. INFO.:			US 1974-523293	19741113
			US 1975-543558	19750123

GI



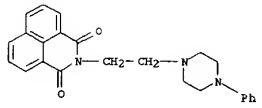
I

AB Benzisoquinolinediones (I, R = Ph, p-MeO-, o-MeOC6H4, p-Cl-, o-ClC6H4, m-F3CC6H4, p-FC6H4, PhCN2) were obtained as their hydrochlorides by treatment of naphthalic anhydride with H2NCH2CH2OH to give a hydroxyethylbenzisoquinolinedione which was treated with p-MeC6H4-SO2Cl to give a sulfonate ester followed by treatment with the corresponding piperazine deriv. I were useful as antidepressants and inflammation inhibitors.

IT **58895-65-1P 58895-66-2P 58895-67-3P 58895-68-4P 58895-69-5P 58895-70-8P 58895-71-9P 58895-76-4P 58895-78-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

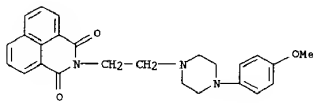
RN 58895-65-1 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



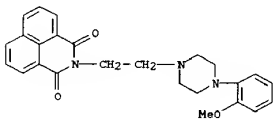
● 2 HCl

RN 58895-66-2 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

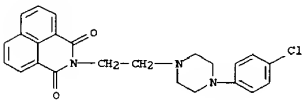
RN 58895-67-3 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

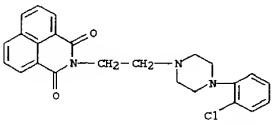
RN 58895-68-4 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

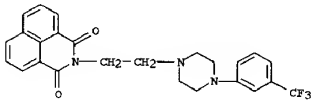


● HCl

RN 58895-69-5 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



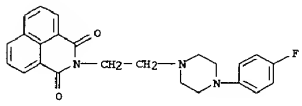
RN 58895-70-8 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

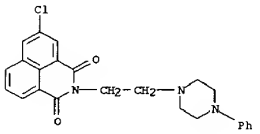
RN 58895-71-9 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



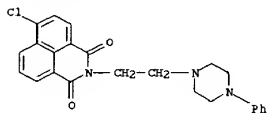
● HCl

RN 58895-76-4 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 58895-78-6 CAPLUS
CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 6-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



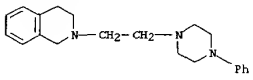
● HCl

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 249 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:59553 CAPLUS
DOCUMENT NUMBER: 84:59553
TITLE: Heterocyclic derivatives of substituted 1-alkyl-4-phenylpiperazine
INVENTOR(S): Giannini, Mario
PATENT ASSIGNEE(S): MALESCI S.a.S. Istituto Farmacobiologico, Italy
SOURCE: Belg., 31 pp.
CODEN: BEXXAL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 820242	A2	19750116	BE 1974-2053876	19740924
CH 624402	A	19810731	CH 1974-11406	19740821

PRIORITY APPLN. INFO.: IT 1974-48923 19740301
GI For diagram(s), see printed CA Issue.
AB Antihypertensive (no data) piperazines I were prepd. Thus, I (R = 4-imidazolyl, R1 = H, R2 = H, 2-Me, 4-Me, 2-Cl, 2-OMe, 4-Cl, 4-OMe, n = 0; R = 2-pyridyl(py), 3-py, 4-py, R1 = R2 = H, n = 0; R = 3-py, R1 = H, R2 = H, 2-OMe, 2-Cl, n = 1; R = 3-py, R1 = R2 = H, n = 2; R = 1,2,3,4-tetrahydro-2-isoquinolyl, R1 = R2 = H, n = 1; R = 2-methyl-1,2,3,4-tetrahydro-3-isoquinolyl, R1 = R2 = H, n = 0) were prepd. by treating N-arylpiperazines (II) with R(CH2)n+1Cl. I (R = 3-py, R1 = OH, R2 = H, 2-OMe, 3-OMe, 4-OMe, 2-Me, 3-Me, 4-Me, 2-Cl, 3-Cl, 4-Cl, 2-F, n = 1; R = 4-py, R1 = OH, R2 = H, 2-OMe, n = 1) were prepd. by treating II with RCOCH2Br and reducing the ketone in situ with NaBH4. I (R = 3-py, R1 = OMe, OEt, R2 = H, 2-OMe, 2-Cl, n = 1) were obtained by alkylating I (R1 = OH).
IT **58013-22-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 58013-22-2 CAPLUS
CN Isoquinoline, 1,2,3,4-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 249 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

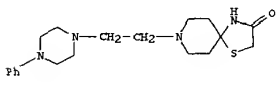
L14 ANSWER 250 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:44001 CAPLUS
DOCUMENT NUMBER: 84:44001
TITLE: Spirocyclic compounds
INVENTOR(S): Nakanishi, Michio; Arimura, Katsuo; Tsing, In Mu
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: Japan., 4 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49028195	B4	19740724	JP 1970-4618	19700117

GI For diagram(s), see printed CA Issue.
AB Twenty-six thiadiazaspiro compds. (I, n = 2, 3, R = Me, m-CF3C6H4, p-ClC6H4, etc., R1 = Me2N, Et2N, morpholino, H2N, 3-piperidinyl etc.,) or their hydrochlorides or maleates, useful as antispasmodics, analgesics, and sedatives, (no data) were prepd. by reacting the appropriate 1-(aminoalkyl)-4-piperidinone with HSCH2CO2H and (NH4)2CO3 (for I where R1 = H2N) or with RH. E.g., 18.4 g 1-[3-(dimethylamino)propyl]-4-oxopiperidine was refluxed with 14.5 g (NH4)2CO3 and 11 g HSCH2CO2H in 400 ml benzene for 15 hr to give 14 g I (n = 3, R = H, R1 = Me2N).cntdot.2HCl. II was prepd. similarly.
IT **54950-45-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 54950-45-7 CAPLUS
CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- , (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 54950-44-6
CMF C19 H28 N4 O S

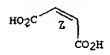


CM 2

CRN 110-16-7

L14 ANSWER 250 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.



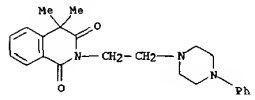
L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1975:443207 CAPLUS
DOCUMENT NUMBER: 83:43207
TITLE: 2-(Piperazinylalkyl)isoquinolinediones
INVENTOR(S): Kutter, Eberhard; Austel, Volkhard; Eberlien, Wolfgang; Heider, Joachim
PATENT ASSIGNEE(S): thomae, Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2345422	A1	19750320	DE 1973-2345422	19730908
DE 2345422	C2	19831222		
AT 7406514	A	19751015	AT 1974-6514	19740808
AT 330777	B	19760726		
FI 7402465	A	19750309	FI 1974-2465	19740821
FI 52219	B	19770331		
ES 429473	A1	19760901	ES 1974-429473	19740823
US 3948898	A	19760406	US 1974-503072	19740904
SU 528035	D	19760905	SU 1974-2057995	19740904
AU 7473023	A1	19760311	AU 1974-73023	19740905
BE 819651	A1	19750306	BE 1974-148302	19740906
SE 7411312	A	19750310	SE 1974-11312	19740906
SE 424863	B	19820816		
SE 424863	C	19821125		
NO 7403220	A	19750311	NO 1974-3220	19740906
NO 140978	B	19790910		
NL 7411843	A	19750311	NL 1974-11843	19740906
NL 176363	B	19841101		
NL 176363	C	19850401		
FR 2242979	A1	19750404	FR 1974-30387	19740906
DK 7404727	A	19750505	DK 1974-4727	19740906
JP 50050381	A2	19750506	JP 1974-102862	19740906
JP 59006868	B4	19840215		
DD 115122	C	19750912	DD 1974-180966	19740906
HU 167869	P	19751225	HU 1974-TO980	19740906
ZA 7405688	A	19760526	ZA 1974-5688	19740906
GB 1446791	A	19760818	GB 1974-39083	19740906
CH 605778	A	19781013	CH 1974-12189	19740906
CH 605779	A	19781013	CH 1977-16014	19740906
RO 63655	P	19781015	RO 1974-79932	19740906
CS 185660	P	19781031	CS 1974-6150	19740906
PL 91712	P	19770331	PL 1974-173958	19740907
ES 433959	A1	19761116	ES 1975-433959	19750120
ES 433958	A1	19761116	ES 1975-433958	19750120
SU 538664	D	19761205	SU 1975-2145942	19750620
SU 545256	D	19770130	SU 1975-2145935	19750620
AT 7505607	A	19760515	AT 1975-5607	19750721
AT 334375	B	19760110		
AT 7505606	A	19760515	AT 1975-5606	19750721
AT 334374	B	19760110		
US 4021558	A	19770503	US 1976-651568	19760122

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
PRIORITY APPLN. INFO.:

	DE 1973-2345422	19730908
	DE 1973-2345423	19730908
	AT 1974-6514	19740808
	US 1974-503072	19740904

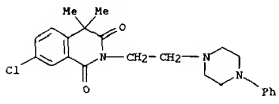
GI For diagram(s), see printed CA Issue.
AB Twenty-five isoquinolinediones I (R = Ph, substituted Ph, or 2-pyridyl; R1 = H or Me; R2 = H, F, Cl, or MeO; n = 2 or 3), useful as antihypertensives or sedatives or in tachycardia treatment (no data), were prepd. by reaction of the isochromandiones (II, X = O) or isoquinolinediones II (X = NH) with (1-piperazinyl)alkylamines or (1-piperazinyl)alkyl chlorides, resp., or by reaction of the isoquinolinediones [II, X = N(CH2)nCl] with the piperazines.
IT **55974-36-2P 55974-37-3P 55974-38-4P 55974-39-5P 55974-40-8P 55974-42-0P 55974-43-1P 55974-45-3P 55974-46-4P 55974-47-5P 55974-48-6P 55974-49-7P 55974-51-1P 55974-52-2P 56010-74-3P 56045-26-2P**
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of antihypertensive and sedative)
RN 55974-36-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

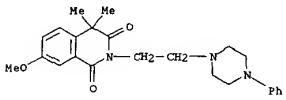
RN 55974-37-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 7-chloro-4,4-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



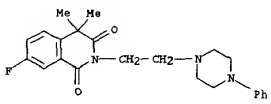
●x HCl

RN 55974-38-4 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 7-methoxy-4,4-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

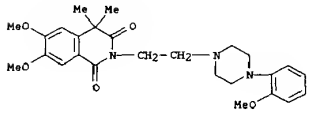
RN 55974-39-5 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 7-fluoro-4,4-diphenyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

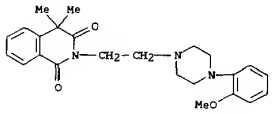
RN 55974-40-8 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 6,7-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



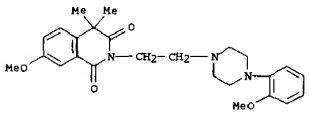
●x HCl

RN 55974-42-0 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

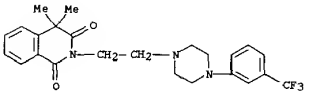
RN 55974-43-1 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 7-methoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

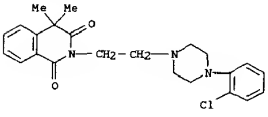
RN 55974-45-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-(3-methyl-4-phenyl-1-

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 55974-48-6 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

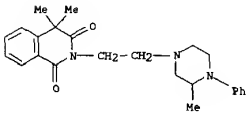
RN 55974-49-7 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

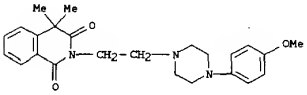
RN 55974-51-1 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(3,4-dimethoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



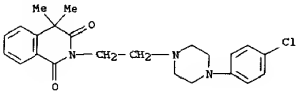
●2 HCl

RN 55974-46-4 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



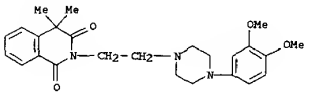
●2 HCl

RN 55974-47-5 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



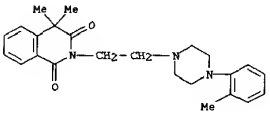
●2 HCl

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



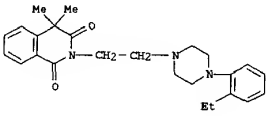
●2 HCl

RN 55974-52-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

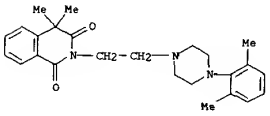
RN 56010-74-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-ethylphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 56045-26-2 CAPLUS

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2,6-dimethylphenyl]-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1975:410049 CAPLUS
DOCUMENT NUMBER: 83:10049
TITLE: Spirocyclic compounds
INVENTOR(S): Arimura, Katsuo; Kohayagawa, Takahiro; Tsing, In Mu; Tsuda, Yoshiaki
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd.
SOURCE: Jpn. Tokkyo Koho, 4 pp.
CODEN: JAXXAO
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

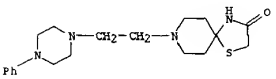
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49029196	B4	19740801	JP 1971-48716	19710702
CH 501635	A	19710115	CH 1968-501635	19680229
NL 6902779	A	19690902	NL 1969-2779	19690221
DK 122725	B	19720404	DK 1969-982	19690221
US 3624075	A	19711130	US 1969-801801	19690224
FR 2002897	A5	19691031	FR 1969-5170	19690227
BE 729209	A	19690828	BE 1969-729209	19690228
AT 286994	B	19710111	AT 1969-2038	19690228
AT 286997	B	19710111	AT 1970-2017	19690228
AT 286996	B	19710111	AT 1970-2014	19690228
ES 364635	A1	19710201	ES 1969-364635	19690228
ES 364633	A1	19710201	ES 1969-364633	19690228
ES 364637	A1	19710201	ES 1969-364637	19690228
ES 364634	A1	19710201	ES 1969-364634	19690228
ES 364632	A1	19710201	ES 1969-364632	19690228
AT 287729	B	19710210	AT 1970-2015	19690228
AT 289815	B	19710510	AT 1970-2016	19690228
GB 1259648	A	19720105	GB 1969-1259648	19690228
BR 6906750	A0	19730419	BR 1969-206750	19690228
JP 49027876	B4	19740722	JP 1969-14996	19690228
JP 49029197	B4	19740801	JP 1971-48717	19710702

PRIORITY APPLN. INFO.: CH 1968-3055 19680229
GI For diagram(s), see printed CA Issue.
AB Forty-three I [(R = Me2NCH2CH2, Me2N(CH2)3, Et2N(CH2)2, Et2N(CH2)3, 2-piperidinoethyl, 3-morpholinopropyl, etc.; R1 = H, Me; R2 = Ph, H, Et, C6H4CF3-m, C6H4Cl-p, etc.] or their salts, useful as analgesics and tranquilizers (no data), were prepd. from RX (X = halogen) and I (R = H). E.g., 7.6 g I (R = R1 = R2 = H). HBr in 80 ml DMF contg. 10 g Na2CO3 was heated at 80-95.degree. with 4.2 g Me2N(CH2)3Cl, the ppt. obtained dissolved in CHCl3 and washed with satd. aq. NaCl soln. to give 4 g I [R = Me2N(CH2)3, R1 = R2 = H].cntdot.2HCl.
IT **54950-45-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 54950-45-7 CAPLUS
CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]-

L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

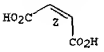
CRN 54950-44-6
CMF C19 H28 N4 O S



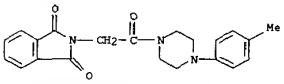
CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

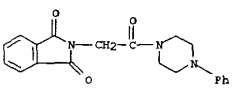
Double bond geometry as shown.



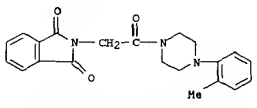
L14 ANSWER 253 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:505444 CAPLUS
DOCUMENT NUMBER: 81:105444
TITLE: Possible antiparkinsonian compounds. I. Synthesis of N-aryl/alkyl-N'-phthaloyl glycyl/dl-.alpha.-(-alanyl)piperazines
AUTHOR(S): Tiwari, S. S.; Pandey, V. K.
CORPORATE SOURCE: Dep. Chem., Lucknow Univ., Lucknow, India
SOURCE: Indian J. Appl. Chem. (1972), 35(4-6), 85-6
CODEN: IJACAN
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The piperazines I (R = Ph, p-MeC6H4, Me, p-ClC6H4, etc.; R1 = H, Me) were prepd. by treating phthaloylacyl chlorides with piperazines.
IT **53646-59-6P 53646-60-9P 53646-61-0P**
53646-62-1P 53646-63-2P 53646-64-3P
53646-65-4P 53646-66-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53646-59-6 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



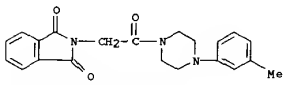
RN 53646-60-9 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



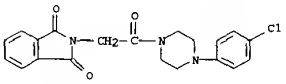
RN 53646-61-0 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



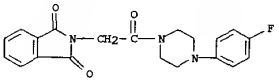
RN 53646-62-1 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



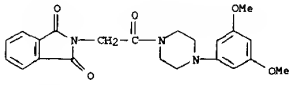
RN 53646-63-2 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]- (9CI) (CA INDEX NAME)



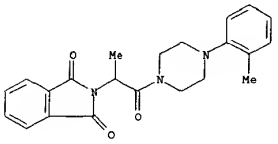
RN 53646-64-3 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 53646-65-4 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



RN 53646-66-5 CAPLUS
CN Piperazine, 1-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxopropyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1974:82731 CAPLUS
DOCUMENT NUMBER: 80:82731
TITLE: 1,2,4,5-Tetrahydro-3H,3-benzazepines
INVENTOR(S): Shetty, Bola V.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: Fr. Demande, 73 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

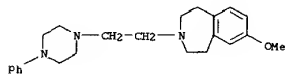
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2171879	A1	19730928	FR 1972-4829	19720214
FR 2171879	B1	19750425		

GI For diagram(s), see printed CA issue.

AB Benzazepines I (R = CH2CH:CMe2, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, allyl, 2-(4-phenylpiperazino)-ethyl, CH2CMe:CH2, CN2C.tplbond.CH, Me, Et, Pr, CH2CH2Ph, CHMeCH2Ph, CH2CH2C6H4NH2-p, CH2CH2C6H4NHAc-p, CH2CH:CHPh, trans-2-phenylcyclopropylmethyl, CH2CH2OAc, CH2CHMeOAc, CHMeCH2C6H4NH2-p) were prepd. by substitution of I (R = H). I (R = H, R1 = Me) was prepd. by methylating 3,4-Me2C6H3OH, oxidizing the 3,4-Me2C6H3OMe, converting the 4-MeOC6H4(CO2H)2-1,2 to its anhydride, reducing to 4-MeOC6H4(CH2OH)2-1,2, and converting to 4-MeOC6H4(CH2Br)2-1,2 and 4-MeOC6H4(CH2CN)2-1,2, which was cyclized to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with BH3. Demethylation with HBr gave 1 (R = R1 = H). 1 are analgesics and narcotic antagonists. Thus, I (R = CH2CH2C6H4NHAc-p, R1 = Me) had an oral ED50 in the writhing test of 32 mg/kg.

IT **36134-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

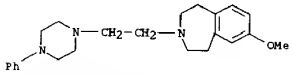


●2 HCl

L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:526338 CAPLUS
DOCUMENT NUMBER: 79:126338
TITLE: 1,2,4,5-Tetrahydro-3H-3-benzazepines
INVENTOR(S): Shetty, Bola V.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: Ger. Offen., 82 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

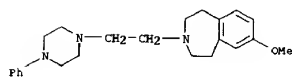
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2207430	A1	19730823	DE 1972-2207430	19720214
DE 2207430	B2	19810723		
DE 2207430	C3	19820513		

GI For diagram(s), see printed CA Issue.
AB Benzazepines I (R = H, CH2CH:CMe2, CH2CMe:CH2, CH2CH:CHPh, allyl, CH2C.tplbond.CH, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, trans-2-phenylcyclopropylmethyl, Me, Et, Pr, CH2CH2Ph, CHMeCH2Ph, CH2CH2C6H4NH2-p, CHMeCH2C6H4NH2-p, CH2CH2C6H4NHAc-p, CH2CH2OAc, (CH2)3OAc, 4-phenylpiperazinylethyl; R1 = H, Me) were prepd. Thus, 3,4-Me2C6H3OH was methylated and oxidized to give 3,4-(HO2C)2C6H3OMe, whose anhydride was reduced to 3,4-(HOCH2)2C6H3OMe, brominated to 3,4-(BrCH2)2C6H3OMe, treated with NaCN to give 3,4-(NCCH2)2C6H3OMe, which was cyclized with HBr-HOAc to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with B2H6 to I (R = H, R1 = He) from which the other I were derived. I demonstrated antihistaminic, analgesic, anticholinergic, and morphine antagonist activity.
IT **36134-35-7P 36134-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 36134-35-7 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

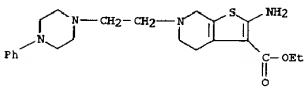


●2 HCl

L14 ANSWER 256 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:466340 CAPLUS
DOCUMENT NUMBER: 79:66340
TITLE: Aminoalkylthienopyridine derivatives
INVENTOR(S): Nakanishi, Michio; Tahara, Tetsuji
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd.
SOURCE: Jpn. Tokkyo Koho, 5 pp.
CODEN: JAXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 48015957	B4	19730518	JP 1969-104694	19691224

GI For diagram(s), see printed CA Issue.
AB The title derivs. I, useful as antiinflammatory and antidiuretic remedies, were prepd. E.g., a mixt. of 1-(2-dimethylaminoethyl)-4-piperidone, CNCH2CO2Et, and S in EtOH was kept 1.5 hr at 60-70.degree., cooled, and (CO2H)2 in EtOH added to give 63.2% I dioxalate (R = Me, R1 = EtCO2, n = 2). Similarly, the following I were prepd. (R, R1, n given): piperidino, EtCO2, 3; pyrrolidino, EtCO2, 3; Et, EtCO2, 2; morpholino, NH2CO, 2; Me, EtCO2, 3; Et, CN, 2; morpholino, EtCO2, 2; 4-phenyl-1-piperazinyl, EtCO2, 2; piperidino, Bz, 3; and pyrrolidino, BuCO2, 3.
IT **42026-24-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 42026-24-4 CAPLUS
CN Thieno[2,3-c]pyridine-3-carboxylic acid, 2-amino-4,5,6,7-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

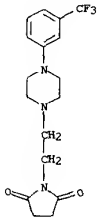


L14 ANSWER 257 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:159666 CAPLUS
DOCUMENT NUMBER: 78:159666
TITLE: Anorexigenic 1-ethyl-4-[m-(trifluoromethyl)phenyl]piperzine derivatives
INVENTOR(S): Cross, Peter E.
PATENT ASSIGNEE(S): Pfizer Corp.
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2242382	A1	19730315	DE 1972-2242382	19720829
AU 7245940	A1	19740228	AU 1972-45940	19720824
NL 7211694	A	19730306	NL 1972-11694	19720828
BE 788280	A1	19730228	BE 1972-121582	19720831
FR 2154449	A1	19730511	FR 1972-31080	19720901
CH 551430	A	19740715	CH 1974-3568	19720901
CH 554899	A	19741015	CH 1972-12935	19720901
AT 320655	B	19750225	AT 1973-10895	19720901
AT 321307	B	19750325	AT 1972-7520	19720901
JP 48085584	A2	19731113	JP 1972-88020	19720904
ES 406374	A1	19750716	ES 1972-406374	19720904
PRIORITY APPLN. INFO.:			GB 1971-41322	19710904
			GB 1972-20536	19720503

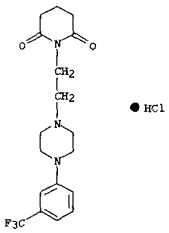
GI For diagram(s), see printed CA Issue.
AB Eight title compds. (I, R = H, Cl, or Br; R1 = e.g. succinimido, glutarimido, or 2,4-dioxo-3-imidazolidinyl) and (or) their HCl salts were prepd. and used as appetite depressants. Thus, 11.5 g 1-[m-(trifluoromethyl)-phenyl]piperazine, 8.1 g .beta.-succinimidoethyl chloride, K2CO3, and MeI were heated in DMF for 24 hr at 100.degree. to give 9.1 g I.HCl (R = H, R1 = succinimido).
IT **41212-97-9P 41212-99-1P 41213-05-2P**
41213-07-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 41212-97-9 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 257 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

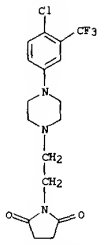
RN 41212-99-1 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

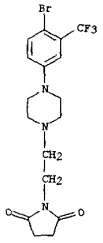
RN 41213-05-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[4-chloro-3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 257 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



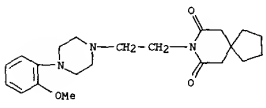
● HCl

RN 41213-07-4 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[4-bromo-3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 258 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:443062 CAPLUS
DOCUMENT NUMBER: 77:43062
TITLE: Psychosedative agents. 2. 8-(4-Substituted 1-piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones
AUTHOR(S): Wu, Yao-Hua; Rayburn, J. W.; Allen, L. E.; Ferguson, H. C.; Kissel, J. W.
CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville, Indiana, USA
SOURCE: J. Med. Chem. (1972), 15(5), 477-9
CODEN: JMCMAR
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several of the title compds. synthesized had greater potency and selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus, 2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione (I) [33386-08-2] had an ED50 for complete suppression of conditioned avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was required for complete suppression of the unconditioned escape response. Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8 and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less sedation than chlorpromazine, had very little .alpha.-adrenergic blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p. in mice. The incidence of catalepsy induced by I in monkeys was similar to that with chlorpromazine. To synthesize I, N-(2-pyrimidinyl)piperazine was prepd. from piperazine and 2-chloropyrimidine by nucleophilic aromatic substitution, reacted with .omega.-chloropropionitrile, reduced with LiAlH4 or Raney Ni-H2 to 1-(.omega.-aminobutyl)-4-(2-pyrimidinyl)piperazine, and reacted with the spiro compd. cyclopentane-1,1-diacetic acid anhydride.
IT 21102-95-4
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(tranquilizing activity of)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 258 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

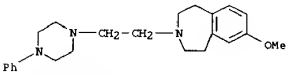


●2 HCl

L14 ANSWER 259 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:153628 CAPLUS
DOCUMENT NUMBER: 76:153628
TITLE: 1,2,4,5-Tetrahydro-3H-3-benzazepines as analgesics and
antagonists of narcotics
PATENT ASSIGNEE(S): Wallace and Tiernan, Inc.
SOURCE: Brit., 42 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

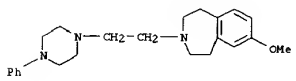
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1268243		19720322		

PRIORITY APPLN. INFO.: US 1968-711897 19680311
GI For diagram(s), see printed CA Issue.
AB H-3-Benzazepines (I, R was usually 7- or 8-MeO or 7-OH; R1 was, e.g., H,
alkyl, cycloalkylmethyl, substituted phenethyl, p-MeC6H4SO2, a cetoxyalkyl; R2 = H3 Me), useful as analgesics, anticholinergics, antihistamines, and antagonists to narcotics, were prepd. Thus, 50 g 4-methoxy-.omicron.-benzenediacetimide (II) was reduced by borane in THF
at 10.degree. to give 28 g I (R = 7-MeO, R1 = R2 = H), analyzed as the
maleate. II was prepd. from 3,4-dimethylphenol by methyla-tion, oxidn. to
4-methoxyphthalic acid, formation of the an-hydride, redn. to
4-methoxy-.omicron.-xylene-.alpha.,.alpha.'-diol, dibromination of the
diol, conversion to the dinitrile, and cyclization to the imide. Pharmacol. test results were given.
IT **36134-35-7P 36134-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 36134-35-7 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 259 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

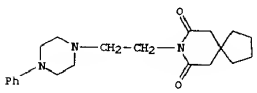


●2 HCl

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1971:125435 CAPLUS
DOCUMENT NUMBER: 74:125435
TITLE: Pharmacologic compositions containing azaspirodecanediones and azaspiroundecanediones
INVENTOR(S): Wu, Yao Hua
PATENT ASSIGNEE(S): Mead Johnson and Co.
SOURCE: U.S., 6 pp. Continuation-in-part of U.S. 3,398,151
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3558777	A	19710126	US 1968-738848	19680621

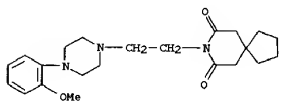
AB The disclosure is similar, but the claims are different.
IT **21090-06-4P 21102-95-4P 21102-99-8P**
25024-82-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 21090-08-4 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

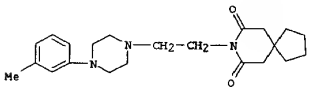
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



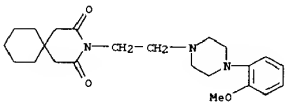
●2 HCl

RN 21102-99-8 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 25024-82-2 CAPLUS
CN 1,1-Cyclohexanediacetimide, N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

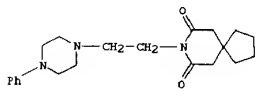
RS1.551.

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1969:500204 CAPLUS
DOCUMENT NUMBER: 71:100204
TITLE: Psychosedative agents. N-(4-phenyl-1-piperazinylalkyl)-substituted cyclic imides
AUTHOR(S): Wu, Yao-Hua; Smith, Kenneth R.; Rayburn, James W.; Kissel, John W.
CORPORATE SOURCE: Dep. Pharmacol., Mead Johnson Res. Center, Evansville, Indiana, USA
SOURCE: J. Med. Chem. (1969), 12, 876-81
CODEN: JMCMAR
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fifty-two N-substituted cyclic imides bearing a 4-phenyl-1-piperazinylalkyl moiety were synthesized and screened as psychosedative agents. The results of 2 test methods, (a) antagonism of amphetamine-aggregation stress in mice and (b) suppression of the conditioned avoidance response in rats, indicate that these compds. possess in varying degrees psychotropic properties typical of major tranquilizers.

IT **21090-08-4 21102-95-4 21102-99-8 21103-15-1 21103-17-3 21103-21-9 21103-24-2 25024-54-8 25024-66-2 25024-74-2 25024-76-4 25024-82-2 25024-84-4 25024-90-2 25024-91-3 25024-92-4 25024-93-5 25024-94-6**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(tranquilizing activity of)

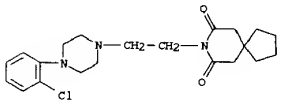
RN 21090-08-4 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

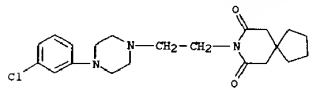
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



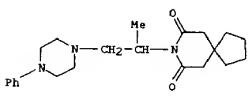
● HCl

RN 21103-21-9 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

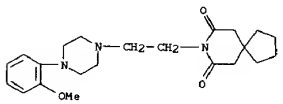
RN 21103-24-2 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

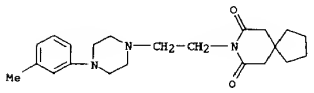
RN 25024-54-8 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-o-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



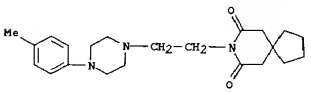
●2 HCl

RN 21102-99-8 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

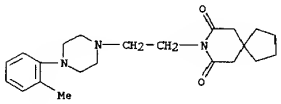
RN 21103-15-1 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

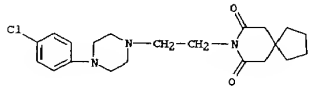
RN 21103-17-3 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



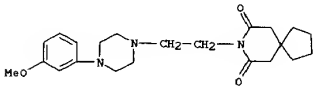
● HCl

RN 25024-66-2 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(p-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



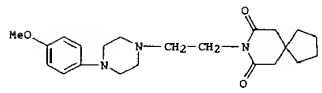
● HCl

RN 25024-74-2 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



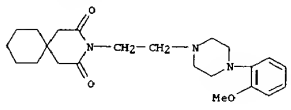
● HCl

RN 25024-76-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



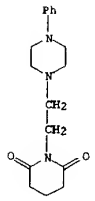
● HCl

RN 25024-82-2 CAPLUS
CN 1,1-Cyclohexanediacetimide,
N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-
, monohydrochloride (8CI) (CA INDEX NAME)



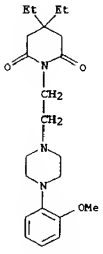
● HCl

RN 25024-84-4 CAPLUS
CN Glutarimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride
(8CI)
(CA INDEX NAME)



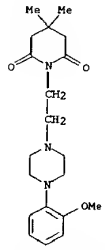
● HCl

RN 25024-90-2 CAPLUS
CN Glutarimide,
3,3-diethyl-N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-,
monohydrochloride (8CI) (CA INDEX NAME)



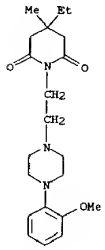
● HCl

RN 25024-91-3 CAPLUS
CN Glutarimide,
N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl-,
dihydrochloride (8CI) (CA INDEX NAME)



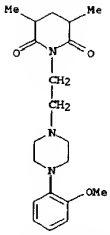
●2 HCl

RN 25024-92-4 CAPLUS
CN Glutarimide,
3-ethyl-N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-3-
methyl-, dihydrochloride (8CI) (CA INDEX NAME)

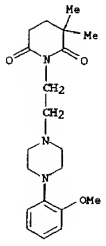


●2 HCl

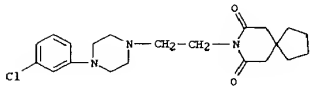
RN 25024-93-5 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-
dimethyl- (9CI) (CA INDEX NAME)



RN 25024-94-6 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-
dimethyl- (9CI) (CA INDEX NAME)

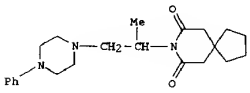


L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

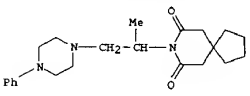


● HCl

RN 21103-23-1 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]- (8CI) (CA INDEX NAME)



RN 21103-24-2 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]- , dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 263 OF 263 CAPLUS COPYRIGHT 2002 ACS

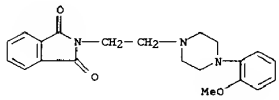
ACCESSION NUMBER: 1968:410474 CAPLUS
DOCUMENT NUMBER: 69:10474
TITLE: Preparation of phthalimidoalkyl piperazines
INVENTOR(S): Lavrinovics, E.; Grinsteins, V.
SOURCE: U.S.S.R.
CODEN: URXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 193524		19670313	SU	19660407

AB From Izobret., Prom. Obraztsy, Tovarnye Znaki 1967, 44(7), 39. N-Arylpiperazine is treated with N-haloalkylphthalimide in MeOH under reflux to yield the title compds.

IT **18503-07-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 18503-07-6 CAPLUS
CN Phthalimide, N-[[4-(o-methoxyphenyl)-1-piperazinyl]methyl]-, monohydrobromide (8CI) (CA INDEX NAME)



● HBr

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1969:4143 CAPLUS
DOCUMENT NUMBER: 70:4143
TITLE: Azaspirodecanediones and azaspiroundecanediones
INVENTOR(S): Wu, Yao Hua
PATENT ASSIGNEE(S): Mead Johnson and Co.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3398151	A	19680820	US 1967-607908	19670109

GI For diagram(s), see printed CA Issue.
AB 8-(4-Phenyl-1-piperazinylalkylene)-8-azaspiro[4.5]decane-7,9-diones [I, n = 2, A = (CH2)x] having 0-3 substituents in the Ph ring were synthesized from the corresponding 4-phenylpiperazines and 3,3-tetramethyleneglutaric anhydride (II). Employing 3,3-pentamethyleneglutaric anhydride in the method yielded the 3-azaspiro[5.5]undecane-2,4-dione analog. These substances have strong activity and good selectivity in suppressing conditioned avoidance response in animals and are useful as psychotropic agents, analgetics, centrally acting muscle relaxants, capillary protectants, antiallergic agents, anti-inflammatory agents, and antiemetics. Thus, a mixt. of 0.1 mole of the substituted glutaric anhydride, 0.1 mole 1-(.omega.-aminoalkyl)-4-phenylpiperazine, and 400 ml. C5H5N was refluxed 15 hrs., the solvent distd., and the residue purified by distn. in vacuo or crystn. If the residue contained amide and carboxyl bands in the ir, it was refluxed with 10 parts by wt. Ac2O for 15 hrs. prior to purification as above. The HCl salt of the free base was prepd. by treating the EtOH soln. of the free base with an equiv. amt. of ethanolic HCl soln. The following I were thus obtained (n A, R, b.p./mm., % yield, m.p. of HCl salt, and crystn. solvent given): 4, (CH2)2, H 215-35.degree./0.45, 80, 135-7.degree. (decompn.), iso-PrOH; 4, (CH2)3, H, 250-2.degree./0.5, 80, 234.5-6.5.degree. (decompn.), iso-PrOH-EtOH; 4, (CH2)4, H, 260-75.degree./0.1, 82.8, 218.5-20.5.degree. (decompn.), iso-PrOH; 4, (CH2)5, H, 253-63.degree./0.2, 89, 188.5-96.5, EtOH; 5, (CH2)3, H, 263-76.degree./0.15-0.25, 77.8, 254-5.degree. (decompn.), EtOH; 5, (CH2)2, o-He, 230-60.degree./0.2, 92, 211-12.degree. (decompn.), EtOH; 4, (CH2)2, o-He (III), 220-40.degree./0.35, 77, 196.5-8.5.degree.

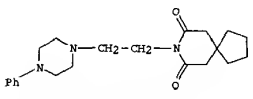
L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(decompn.), EtOH); 4, (CH2)3, o-Me, 220-50.degree./0.11, 90, 208.5-10.5.degree. (decompn.), iso-PrOH; 4, (CH2)2, m-Me, 225-35.degree./0.3, 81, 205.5-7.0.degree. (decompn.), iso-PrOH; 4, (CH2)3, o-Cl, 215-45.degree./0.1, 94, 234.5-5.5.degree. (decompn.), iso-PrOH; 4, (CH2)3, m-OMe, 200-60.degree./0.1, 70, 235.5-7.0.degree. (decompn.), EtOH; 4, (CH2)2CHMeCH2, H, 235-50.degree./0.25, 80, 207.5-12.0.degree., iso-PrOH; 4, (CH2)4, o-OMe, 243-7.degree./0.18, 89.6, 199.5-203.degree., EtOH; 4, (CH2)4, o-Cl, 240-60.degree./-0.2, 90, 238.5-41.0.degree., EtOH; 4, (CH2)4, o-He, 230-70.degree./0.1, 95, 202-3.5.degree., EtOH; 4, (CH2)4, o-Me, 255.degree./0.01, 86, 246-7.5.degree., EtOH; 4, (CH2)3, o-Me, 230-50.degree./0.3, 90, 254.5-5.5.degree. (decompn.), iso-PrOH; 4, (CH2)5, o-OMe, -, 88, 174.5-6.5.degree., EtOH-Et2O; 4, (CH2)3, p-He, 160-80.degree./0.1, 75, 247-8.degree. (decompn.), iso-PrOH; 4 (CH2)2, p-Me, 165-200.degree./0.05-0.1, 73, 236.5-8.5.degree. (decompn.), iso-PrOH; 4, (CH2)2, o-Cl, 165-84.degree./0.1, 80, 241-2.5.degree. (decompn.), iso-PrOH; 4, (CH2)3, m-Cl, 164-70.degree./0.1, 68, 248.5-50.5.degree. (decompn.), iso-PrOH; 4, (CH2)2, m-Cl, 140-210.degree./0.5-0.1, 74, 226.5-8.5.degree. (decompn.), iso-PrOH; 4, (CH2)3, p-Cl, 175-97.degree./0.1, 90, 248-9.degree. (decompn.), EtOH; 4, CHMeCH2, H, 230-40.degree./0.25, 87, 255.5-7.5.degree., EtOH. A stirred mixt. of 19.2 g. 1-(o-methoxyphenyl)-piperazine (IV), 9.0 g. ClCH2CH2CN, 150 ml. C6H6, and 16.6 g. anhyd. Na2CO3 was refluxed overnight under anhyd. conditions and filtered, the filter cake washed with C6H6, and the combined C6H6 filtrates fractionally distd. in vacuo to give 19.6 g. 1-(2-cyanoethyl)-4-(o-methoxyphenyl)piperazine (V), bl 208-26.degree., m. 72-4.degree.. A mixt. of 8.1 g. V, 30 g. dry liq. NH3, and 100 ml. abs. MeOH was hydrogenated at 1200 psi. and room temp. over W-6 Raney Ni to give 95% 1-(3-aminopropyl)-4-(o-methoxyphenyl)piperazine (VI, A = (CH2)3, R = o-MeO). The following VI were similarly prepd. (except that the last five compds. were prepd. by redn. with LiAlH4, an example of which is given below) (A, R, % yield, b.p./mm., and n25D given): (CH2)2, m-Me, 85.5, 117-34.degree./0.3, 1.5638; (CH2)3, m-OMe, 68.8, 115-65.degree./0.15, 1.5561; (CH2)3, m-Me, 48.0, 120.degree./0.18, 1.5656; (CH2)3, m-Cl, 79, 142-70.degree./0.15-0.5, -; (CH2)3, m-Cl, 62, 108-40.degree./0.1-0.15, 1.5827; (CH2)2CHMeCH2, H, 81.7, 138-55.degree./0.17, 1.5485; (CH2)4, o-MeO, 79.6, 150-60.degree./0.25, 1.5496; (CH2)4, o-Cl, 74.0, 130-65.degree./0.15-0.35, 1.5560; (CH2)4, o-Me, 32.8, 145-60.degree./0.08, -; (CH2)5, o-MeO, 57.6, 163-72.degree./0.2, 1.5444. 1-(3-Cyano-2-methylpropyl)-4-

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
phenylpiperazine, b0.15 155-68.degree., m. 81-3.degree., prepd. in 65% yield from 3-chloro-2-methylbutyronitrile by the above procedure, was dissolved (0.04 mole) in 100 ml. tetrahydrofuran, the soln. added dropwise with vigorous stirring during 35 min. to a suspension of 1.87 g. LiAlH4 in 100 ml. Et2O and refluxed, and the residue distd. in vacuo to give 81.7% 1-(4-amino-2-methylbutyl)-4-phenylpiperazine, b0.17 138-55.degree., n25D 1.5485. A stirred mixt. of 16.8 g. 11 and 200 ml. C5H5N was treated with 12.2 g. ethanolamine, refluxed 3 hrs., and fractionally distd. in vacuo to give 12.0 g. 8-(2-hydroxyethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII, A = (CH2)2, X = OH)] (VIIa), b0.05-0.1 142-50.degree., n25D 1.5150. A cooled mixt. (10-15.degree.) of 6.0 g. VIIa, 50 ml. C6H6, and 2.4 g. C5H5N was treated dropwise during 25 min. with 3.6 g. SOCl2, heated 1 hr. at 60-5.degree., and filtered, the filtrate treated with 20 ml. distd. H2O, and the C6H6 layer sepd., dried, and fractionally distd. in vacuo to give 4.5 g. 8-(2-chloroethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII, A = (CH2)2, X = Cl)] (VIIb), b0.05 120-2.degree., n25D 1.5139. The following VII were similarly prepd. (A, X, b.p./mm., and % yield given): (CH2)3, OH, 155-70.degree./0.1-0.15, 62; (CH2)3, Cl, 155-62.degree./0.06, 73; (CH2)2O(CH2)2, OH, 191-204.degree./0.08-0.18, 80.7; (CH2)2O(CH2)2, Cl, 155-65.degree./0.25, 50; (CH2)4, OH, 185-240.degree./0.2, 74.9; (CH2)4, Cl, 160-95.degree./0.3, 53.5. A mixt. of 23 g. VIIb, 19.2 g. IV, and 31.8 g. anhyd. Na2CO3, in 400 ml. C6H6 was refluxed 15 hrs., and filtered, and the filtrate fractionally distd. to give III. The following I were similarly prepd. (n, A, R, b.p./mm., % yield, and m.p. of HCl salt given): 4, (CH2)3, p-MeO, 220-45.degree./0.1, 65, 225.5-6.5.degree. (decompn.); 4, (CH2)2O(CH2)2, o-MeO, 240-60.degree./0.2, 20, 206.5-8.5.degree.; 4, (CH2)2O(CH2)2, H, 190-260.degree./0.25-0.35, 86, 155-7.degree.; 4, (CH2)3, m-Me, 160-85.degree./0.5-0.1, 92, 240.5-2.5.degree. (decompn.); 4, (CH2)3, H, 240-60.degree./0.2, 69, 217.5-18.5.degree.; 4, (CH2)4, o-F, -, -, 188-90.degree.; 4, (CH2)4, o-MeSO2NH, -, 73.5, 263.5-4.5.degree.; 4, (CH2)4, o-NO2, 150-80.degree./0.1, 26.8, -. I contg. multiple substituents in the Ph ring were similarly prepd. and were tabulated but not characterized. A mixt. of 15.28 g. II, 200 ml. C5H5N, and 5.0 g.

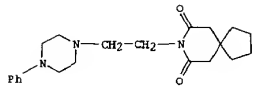
L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
propargylamine was refluxed overnight in the absence of moisture and fractionally distd. in vacuo (b0.15 129-45.degree.) to give crude 8-propargyl-8-azaspiro[4.5]decane-7,9-dione (VIII) contaminated with II.
A mixt. of 6.0 g. VIII, 2.4 g. 37% aq. HCHO, a few crystals of CuCl (catalyst), 1.78 g. AcOH, 2.9 g. distd. H2O, and 4.8 g. 1-phenylpiperazine was heated under N on a water bath at 40.degree. 7 hrs., extd. with 3 .times. 75 ml. CHCl3, and worked up in the usual manner, and the product converted to the HCl salt to give 6.5 g. 8-[4-(4-phenyl-1-piperazinyl)-2-butynyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 173-4.degree. (EtOH). Similarly prepd. was 8-[4-(4-o-methoxyphenyl-1-piperazinyl)-2-butynyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 172-5.degree.

IT **21090-07-3P 21090-08-4P 21102-92-1P**
21102-93-2P 21102-94-3P 21102-95-4P
21102-98-7P 21102-99-8P 21103-14-0P
21103-15-1P 21103-16-2P 21103-17-3P
21103-20-8P 21103-21-9P 21103-23-1P
21103-24-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 21090-07-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

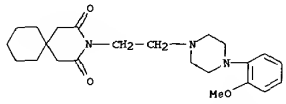


RN 21090-08-4 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

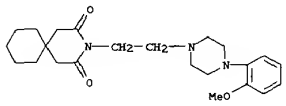


● HCl

RN 21102-92-1 CAPLUS
CN 1,1-Cyclohexanediacetimide, N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- (8CI) (CA INDEX NAME)

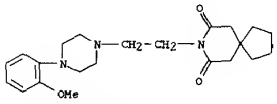


RN 21102-93-2 CAPLUS
CN 1,1-Cyclohexanediacetimide, N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- , hydrochloride (8CI) (CA INDEX NAME)

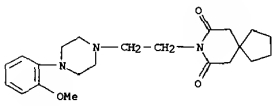


●x HCl

RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 21102-98-7 CAPLUS
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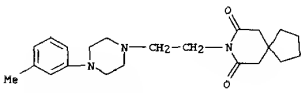
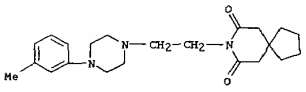
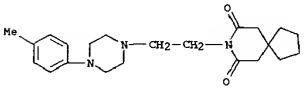


RN 21102-99-8 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

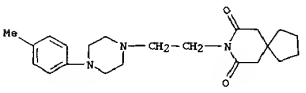


● HCl

RN 21103-14-0 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]- (8CI) (CA INDEX NAME)

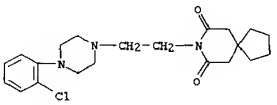


RN 21103-15-1 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

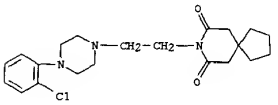


●2 HCl

RN 21103-16-2 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]- (8CI) (CA INDEX NAME)

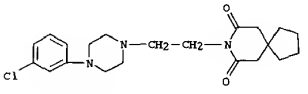


RN 21103-17-3 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]- , monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 21103-20-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 21103-21-9 CAPLUS
CN 1,1-Cyclopentanediacetimide, N-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]- , monohydrochloride (8CI) (CA INDEX NAME)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:443062 CAPLUS
DOCUMENT NUMBER: 77:43062
TITLE: **Psychosedative** agents. 2. 8-(4-Substituted 1-piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones
AUTHOR(S): Wu, Yao-Hua; Rayburn, J. W.; Allen, L. E.; Ferguson, H. C.; Kissel, J. W.
CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville, Indiana, USA
SOURCE: J. Med. Chem. (1972), 15(5), 477-9
CODEN: JMCMAR
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several of the title compds. synthesized had greater potency and selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus, 2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione (I) [33386-08-2] had an ED50 for complete suppression of conditioned avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was required for complete suppression of the unconditioned escape response. Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8 and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less sedation than chlorpromazine, had very little .alpha.-**adrenergic** blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p. in mice. The incidence of catalepsy induced by I in monkeys was similar to that with chlorpromazine. To synthesize I, N-(2-pyrimidinyl)piperazine was prepd. from piperazine and 2-chloropyrimidine by nucleophilic aromatic substitution, reacted with .omega.-chloropropionitrile, reduced with LiAlH4 or Raney Ni-H2 to 1-(.omega.-aminobutyl)-4-(2-pyrimidinyl)piperazine, and reacted with the spiro compd. cyclopentane-1,1-diacetic acid anhydride.

L9 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:260493 CAPLUS
DOCUMENT NUMBER: 126:312328
TITLE: Recent advances in the identification of .**alpha**.1- and .**alpha**.2 adrenoceptor subtypes: therapeutic implications
AUTHOR(S): Hieble, J. Paul; Rufolo, Robert R., Jr.
CORPORATE SOURCE: Div. Pharm. Sci., SmithKline Beecham Pharm., King of Prussia, PA, 19406, USA
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(4), 367-387
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A **review**, with 166 refs. The cloning of multiple subtypes of both .**alpha**.1- and .**alpha**.2-adrenoceptors has renewed interest in the therapeutic application of agents interacting with these **receptors**. Effort has primarily been directed towards the design of uroselective .**alpha**.1-adrenoceptor antagonists for the treatment of benign prostatic hyperplasia (BPH). Evidence is accumulating for the involvement of a novel .**alpha**.1-adrenoceptor, designated as .**alpha**.1L-adrenoceptor, in .**alpha**.1-adrenoceptor-mediated smooth muscle contraction in prostatic and other urogenital tissues. While several antagonists showing a high degree of uroselectivity in animal models have been identified, their clin. superiority over the currently available .**alpha**.1-adrenoceptor antagonists has not yet been demonstrated. It is possible that the interaction with .**alpha**.1-adrenoceptors, as yet uncharacterized subtypes, at nonprostatic sites contributes to the therapeutic activity of this drug class in BPH. The .**alpha**.1-adrenoceptor subtypes involved in the control of vascular tone are currently being evaluated, and the profile of interaction with the various .**alpha**.1-adrenoceptor subtypes may play a key role in the efficacy of cardiovascular drugs such as carvedilol. .**alpha**.2-Adrenoceptor agonists are now being employed for a variety of therapeutic applications, most involving actions on **receptors** with the central nervous system (**CNS**). These agents are useful in the treatment of hypertension, glaucoma, opiate withdrawal and attention deficit hyperactivity disorder (ADHD), and as analgesics and adjuncts to general anesthesia. While subtype selectivity has not yet been applied to the design of new .**alpha**.2-adrenoceptor agonists for these applications, recent gene mutation/knock-out expts. have identified the .**alpha**.2-subtypes involved in some of these actions, and optimization of a therapeutic profile may be possible. Furthermore, the design of agents combining affinities for multiple adrenoceptor subtypes, or the combination of a specific adrenoceptor affinity profile with another pharmacol. action, may offer advantages over mols. selective for an individual adrenoceptor subtype.

L9 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:65995 CAPLUS
DOCUMENT NUMBER: 126:113272
TITLE: Role of prostaglandins in the stimulation of the hypothalamic-pituitary-adrenal axis by **adrenergic** and neurohormone systems
AUTHOR(S): Bugajski, J.
CORPORATE SOURCE: Institute Pharmacology, Polish Academy Sciences, Krakow, Pol.
SOURCE: Journal of Physiology and Pharmacology (1996), 47(4), 559-575
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A **review** with 78 refs. Role of prostaglandins (PGs) in the activation of the hypothalamic-pituitary-adrenal (HPA) axis by the **adrenergic** agonists, ACTH-releasing hormone (CRH) and vasopressin (VP) in rats under basal and social stress conditions was investigated. Systemic or intracerebroventricular (icv) pretreatment with indomethacin powerfully reduced the corticosterone response to icv phenylephrine, an .**alpha**.1-**receptor** agonist, significantly diminished the response to clonidine, an .**alpha**.2-**receptor** agonist, but did not alter the response to isoprenaline,a .beta.-**adrenergic** agonist. Consequently, indomethacin considerably reduced the corticosterone response to noradrenaline, an .**alpha**.1- and .**alpha**.2-**adrenergic** agonist, but did not change the response to adrenaline, a predominant .beta.-**adrenergic** agonist. Thus, prostaglandins considerably mediate the HPA activity stimulated via central .**alpha**.1-and .**alpha**.2-but not .beta.-**adrenergic receptors**. Social crowding stress for 3 days did not affect the corticosterone response to i.p. or icv CRH, but drastically reduced the response to VP. In stressed rats indomethacin did not alter the corticosterone response to CRH but significantly further impaired the diminished by stress corticosterone response to VP. Neither social stress nor endogenous prostaglandins affected the responsiveness of the CRH system. By contrast, both social stress and prostaglandins considerably diminished the HPA response to VP. The above results indicate that both these neurohormone systems have a distinct mode of adaptation and interaction with PG systems during social stress. Interleukins, particularly IL-1.beta. and IL-6, activate the HPA axis. Most immunol. stimuli and interleukins also activate both the central and the peripheral noradrenergic systems. Activation of the HPA axis in vivo depends on the secretion of CRH, an intact pituitary and the ventral **adrenergic** bundle innervating the hypothalamic paraventricular nucleus. Interleukins may cross the blood-brain-barrier or be produced in the **CNS** to stimulate their **receptors** in brain structures involved in the regulation of the HPA axis.

L9 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2002 ACS

L9 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:400953 CAPLUS
DOCUMENT NUMBER: 117:953
TITLE: Electrophysiological consequences of activation of adrenoceptors in the **CNS**
AUTHOR(S): McCormick, David A.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA
SOURCE: Adrenoceptors: Struct., Mech., Funct., [Proc. Manchester Symp. Pharmacol. Adrenoceptors], 3rd (1991)
, Meeting Date 1990, 159-69. Editor(s): Szabadi, Elmer; Bradshaw, Christopher M. Birkhaeuser: Basel, Switz.
CODEN: 57QSAA
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A **review**, with 30 refs., on the electrophysiol. consequences of activation of .**alpha**.1-, .**alpha**.2-, and .beta.-adrenoceptors in the central nervous system (**CNS**).

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ACCESSION NUMBER: 1983:516128 CAPLUS
DOCUMENT NUMBER: 99:116128
TITLE: The physiological role of .**alpha**.-adrenoceptors in the **CNS**: new concepts from single-cell studies
AUTHOR(S): Aghajanian, G. K.; Rogawski, M. A.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06508, USA
SOURCE: Trends Pharmacol. Sci. (1983), 4(7), 315-17
CODEN: TPHSDY; ISSN: 0165-6147
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A **review** with 10 refs., on the synaptic localization and functional classification of .**alpha**.1- and .**alpha**.2-**adrenergic receptors** in the central nervous system.